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Editor:

N. RASHEVSKY

Associate Editors:

H. D. LANDAHL *and* ANATOL RAPOPORT

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SOME SUGGESTIONS FOR A NEW THEORY OF CELL DIVISION

N. RASHEVSKY
COMMITTEE ON MATHEMATICAL BIOLOGY
THE UNIVERSITY OF CHICAGO

A number of shortcomings of the diffusion drag force theory of cell division are pointed out, especially in regard to the difficulties of interpreting mitotic phenomena. As an alternative a different theory is outlined, based on the emphasis of colloidal phenomena in the nucleus. The nucleus is assumed to contain very long molecules, which are disoriented in the resting stage but which become oriented prior and during the mitosis, forming the mitotic spindle. Such an oriented structure is of the nature of a tactoid. The molecular mechanism of the formation of the spindle is outlined, and some equations are derived which suggest possible quantitative verification. The interplay of the molecular forces is assumed also to be responsible for the splitting of the chromosomes. Arrangement of chromosomes in the equatorial plate and their movement to the poles are discussed, and equations describing those phenomena are outlined.

The only quantitative theory of cell division which has been developed somewhat systematically is the diffusion drag force theory (Rashevsky, 1948). That theory has some important achievements to its credit. The theoretical estimations of average cell sizes agree with actual values (*loc. cit.*, chap. xi). The predicted correlation between cell size and rate of metabolism (*loc. cit.*, chap. xi) also leads to a fair quantitative agreement. Light is shed on the experimentally observed correlation between glycolitic coefficient and rates of tissue growth (*loc. cit.*, chap. xv). The most striking success of the theory, perhaps, is exhibited by the remarkable agreement between the theoretically derived elongation curves of freely dividing spherical cells (*loc. cit.*, p. 164; also Landahl, 1942b) and the curves actually observed by R. Buchsbaum and R. R. Williamson (1943). A similar agreement is found for the rate of constriction of the "neck" of a freely dividing cell, derived theoretically by G. Young (*loc. cit.*, p. 148).

Against these advantages, a number of shortcomings must be listed. The principal one is probably the failure of the theory to account for phenomena of mitosis. Another shortcoming is the neglect of the role played by colloidal phenomena during cell division.

In the early development of the theory it was argued that since mitosis,

important as it is, is not a universal accompaniment of cell division, therefore a theory of cell division need not primarily be concerned with a theory of mitosis. A theory of mitosis could be developed as a further elaboration of the fundamental assumptions, by addition of new assumptions, if necessary. Such an elaboration of the basic theory was attempted by N. Rashevsky (*loc. cit.*, chap. xvi), without much success. The assumptions made in *loc. cit.* about the attachments of the fibers to the particles seem rather artificial. The conclusion that H. N. Barber's work (1939) supports the theory that chromosome movements are produced by contraction of quasi-elastic fibers (Rashevsky, 1941) was shown by F. Schrader (1944) to be wrong. Moreover, more and more evidence is accumulating showing that there are no continuous fibers in the mitotic spindle. Especially convincing seems to be the work of G. Östergren (1949) on Luzula. His conclusions are that the spindle is of a nature of a tactoid or liquid crystal, a suggestion also made by J. D. Bernal (1940) and other authors.

It must be remarked that all possibilities accounting for phenomena of mitosis on the basis of the diffusion drag force theory have not been exhausted. The complex interplay of such forces may conceivably produce, without the presence of any fibers, the characteristic stages of mitosis. A theory developed along such lines would, however, seem to require a large number of artificial assumptions *ad hoc*.

The heaviest blow, however, to the line of thought which led to the diffusion drag force theory of cell division is dealt by the recent work of Edward D. DeLamater and his associates (DeLamater, 1952; DeLamater and Hunter, 1951; DeLamater and Mudd, 1951, Mudd, Winterscheid, DeLamater, and Henderson, 1951), who report observations on mitosis in bacteria. If, as these observations may indicate, mitosis is a feature of every cell division, then an adequate theory of cell division should account for mitosis in a natural way, and not through additional elaboration.

The other shortcoming mentioned above, namely, the neglect of colloidal changes, is also serious. A number of workers, in particular D. A. Marsland and his coworkers (Brown, 1934; Marsland and Brown, 1936, 1942; Marsland, 1938, 1939; Pease and Marsland, 1939; Pease, 1941; Marsland, 1942; Rugh and Marsland, 1943; Marsland, 1948; Marsland and Jaffee, 1949), have established a close relation between cell division and the gelation of cell colloids. Such a general relation may be rather naturally explained in terms of the diffusion drag force theory. The expression for the dividing forces [*loc. cit.*, p. 143, eq. (12)] contains the diffusion coefficient D in the denominator. A gelation results in a decrease of D and, therefore, in an increase of the dividing forces. However the details of various observations, notably those of D. C. Pease (1941), on the re-

appearance of asters after reduction of pressure are hard to reconcile with the simple diffusion drag force theory.

In some cases effects of drugs also present difficulties. While the inhibitory effect of some drugs on cell division may be explained by their inhibitory effects on metabolism, in some cases the effects strongly indicate the involvement of colloidal mechanisms. We may mention here the observation of B. Osogoe (1941) that potassium ions result not only in an inhibition of division but in an almost complete reversal of a nearly completed process of division. Potassium surely would not totally inhibit the metabolic processes.

Methodologically the diffusion drag force theory has the following advantage. The diffusion drag forces are present in any metabolizing system, hence in any cell which manifests life. Since, as the theory shows, those forces are sufficient to produce cell division, the theory does represent an economy of thought because it does not introduce any extra assumptions. In view of what was said above, it seems that the diffusion drag force theory of cell division has outlived its usefulness. This conclusion should in no way deprecate the possible importance of diffusion drag forces in biology (cf. Hearon, 1949a, b; 1950a, b, c).

Of other theories, the older work of Rashevsky (*loc. cit.*, chap. xiii), which was based on the concept of variable surface tension, may be mentioned. This concept did seem to have some experimental justification (Spek, 1918). However, though a general theory of division can be developed on this basis and some features of elongation during cell division can be described mathematically (Shimbel, 1946), the theory always contains some indefinite parameters, and no prediction as to size of cells, etc., can be made.

More recently Rashevsky suggested a modification of the diffusion drag force theory by considering simple osmotic pressures, produced by diffusion (Rashevsky, 1949a). This approach has the advantage of leading to a theory of segmentation, a phenomenon in which no marked elongation is involved and which offers some difficulties to the diffusion drag force theory. However the objections which hold against the diffusion drag force theory also hold for this theory.

In another paper Rashevsky (1948b) investigated the possibility that elastic stresses, produced by gelation, could result in the division of a cell. From considerations of the theory of plasticity, through application of Betti's theorem, he arrives at the conclusion that such elastic forces could not result in a continuous elongation and eventual division of the system. Recently, however, Irwin Isenberg (1952) has shown that Rashevsky's conclusion holds only for the case of a homogeneous system with constant

viscosity, for which the classical Betti's theorem has been derived. By generalizing Betti's theorem to heterogeneous systems, Isenberg shows that elongation and division due to elastic stresses may be possible. This important work of Isenberg paves the way to a mathematical theory of cell division based on elastic stresses in colloidal systems.

A large amount of qualitative theorizing has been done concerning electric charges as possible sources of cell division. The psychological background for this theorizing may, perhaps, be found in the rather superficial analogy between some mitotic figures and the models of lines of forces between electrical charges. The main difficulty with the theory of electric forces is that the cell as a whole is electrically neutral. Because of the electrical double-layer nature of the cellular charges, rather strong fields may exist locally within the cell. But the gross effect on the cell as a whole cannot be expected to be sufficiently strong. An estimation of electric forces due to metabolic processes which involve diffusion of ions shows that they are much weaker than the diffusion drag forces (*loc. cit.*, chap. xiii).

In the following we shall very briefly outline a possible new approach to the theory of cell division, which emphasizes both the phenomena of mitosis and the role of colloidal structures.

It has been long known that a cell, deprived of cytoplasm but with nucleus intact, will regenerate the cytoplasm; but an ennucleated cell does not regenerate the nucleus. This suggests that the nucleus is the basic region for biological synthesis, the cytoplasm being formed from the nucleus as a sort of by-product or, rather, second step in this process of synthesis. The work of T. Caspersson (1950) gives rather direct support to this concept. We shall therefore consider the nucleus as the basic element of the cell.

In line with existing evidence (Caspersson, *loc. cit.*) we shall consider that the nucleus contains long chain molecules P of proteins or other substances. We assume that due to intermolecular forces, which may be either of the nature of electric dipoles or of ionic cloud origin (Levine, 1939a, b), these molecular chains P all tend to orient themselves in one direction. Complete orientation corresponds to a minimum of the potential energy ϵ_m. This orientation is opposed by the thermal energy. If m is the number of degrees of freedom of a molecule P, then, in order that the orientation be sufficiently pronounced, we must have

$$|\epsilon_m| \gg \frac{m\,kT}{2}, \tag{1}$$

where k is the Boltzmann constant and T the absolute temperature.

The minimum energy ϵ_m, whatever its precise nature, is in general a function $\epsilon_m(c)$ of the concentration c of different substances present in the nucleus. Ions, especially hydrogen ions, are particularly likely to affect ϵ_m. If acid substances are produced in the nucleus and if c is the concentration of the hydrogen ions, then, for a constant rate c of production, we have

$$c = c_0 + \frac{q r_0^2}{D}, \tag{2}$$

where r_0 is the average linear dimension of the nucleus, D the diffusion coefficient, and c_0 the concentration outside of the nucleus.

If $|\epsilon_m|$ increases with c, so that

$$\frac{d|\epsilon_m|}{dc} > 0, \tag{3}$$

and if c^* denotes the concentration above which inequality (1) is valid, then there exists a critical size r^* above which the P molecules will be oriented. That critical size is determined by

$$c_0 + \frac{q r_0^{*2}}{D} = c^*. \tag{4}$$

From (4) we find

$$r^* = \sqrt{\frac{(c^* - c_0) D}{q}}. \tag{5}$$

If we consider as plausible values $c^* - c_0 \sim 10^{-6}$ gm. cm.$^{-3}$, $q \sim 10^{-6}$ gm. cm.$^{-3}$ sec.$^{-1}$, and $D \sim 10^{-7}$ cm.^{2} sec.$^{-1}$, we find $r^* \sim 10^{-3}$ cm. Thus the orientation will occur in regions which are of the order of magnitude of actual nuclei. In developing the theory it will be necessary to make specific physical assumptions about the nature of the intermolecular forces, and to compute ϵ_m as a function of, let us say, the concentration c of some biologically important ions. Then, from the knowledge of the rates of reactions by which those ions are produced and of the diffusion coefficient, a more refined equation than (5) should be derived.

In an anisotropic structure, consisting of oriented long-chain molecules (Fig. 1), the surface tension at the "poles" p is in general different from that at the "equator" e. We shall assume that the equatorial surface tension γ_e is *greater* than the polar γ_p. This assumption implies an inequality between the intermolecular forces in the longitudinal and transverse directions. Our assumption means that it takes less work to remove a molecule from the equator to infinity than from a pole to infinity. If $f_e(r)$ is

the force acting in the first case and $f_p(r)$ the one acting in the second, and if d_e and d_p are the distances of closest approach in the two cases, then we must have

$$\int_{d_p}^{\infty} f_p(r)\, dr > \int_{d_e}^{\infty} f_e(r)\, dr . \tag{6}$$

Again, the expressions $f_e(r)$ and $f_p(r)$ will be determined by the nature of the forces. Inequality (6) actually implies some inequality or inequalities between the parameters which characterize the mechanism of the intermolecular forces. It will be the task of the theory to investigate under what conditions (6) holds, if plausible assumptions are made about the intermolecular forces (e.g., dipoles or ionic clouds).

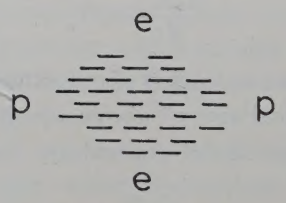


FIGURE 1

We shall consider the chromosomes as bundles of parallel molecular chains which multiply and thus increase in thickness. On the side of each chromosome there is a molecular group C which has a strong affinity for the end of a P molecule. This affinity may be due to a polar character of both the group and of P, or it may be due to other factors. The force of attraction between C and P is assumed to be greater than the force of attraction which holds the individual chains of the chromosome together. If ϵ_c is the minimum value of the binding energy between the chains which constitute the chromosome and ϵ_s the minimum binding energy between C and P, then we assume that

$$\epsilon_c > \epsilon_s . \tag{7}$$

The assumption expressed by inequality (6), namely, $\gamma_e > \gamma_p$, implies that the chromosomes will be arrayed in the equatorial plane along the surface.

If the oriented nuclear structure has a gel-like consistency, then internal stresses will develop in it and it may either be deformed, or simply break in the region of greatest stress. If the gelation and the orientation are related, then the region of maximum stress will be the equatorial region, because the concentration c, which is responsible for the orientation and

gelation, is largest there. If the stress $T(c)$ at the equator is greater than the longitudinal tensile strength S of P,

$$T(c) > S, \tag{8}$$

then the structure simply cracks at the equator. That breaking will partly involve the separation of P molecules and partly the separation of structures like those illustrated in Figure 2, where *Ch* denotes schematically the component chains of a chromosome viewed "end on." Because of inequality (7), the break will occur in this case not between C and P, but between the chains *Ch*. Hence the chromosomes will be split longitudinally, each half belonging to the corresponding "half-spindle."

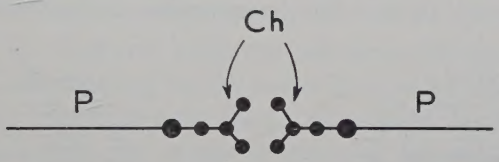


FIGURE 2

The breaking of the spindle results in an increase of its specific surface, and therefore in a decrease of c, which may drop below c^*. When this happens, a *disorientation* occurs in each half-spindle. This disorientation also results in a gradual liquefaction of the structure, which is accompanied by a *reduction of volume*. (A reduction of volume during solation is the rule for cell colloids as evidenced, for example, by the experiments

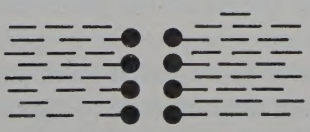


FIGURE 3

mentioned above of Marsland.) This reduction in volume of the two halves will in itself cause a slight initial movement apart of the chromosomes.

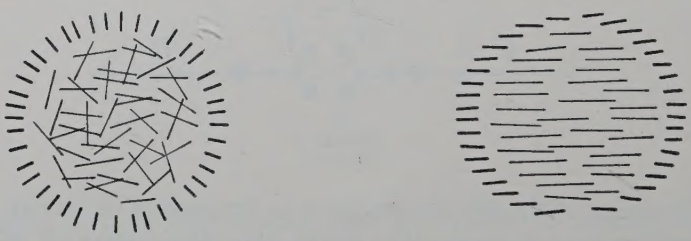
Further movement of the chromosomes may be viewed as due to the fact that they are now arrayed at the "poles" of the half-spindles (Fig. 3). Since the structures are not yet completely disoriented we still shall have, for each half spindle, $\gamma_e > \gamma_p$, though, as the disorientation proceeds,

$\gamma_e - \gamma_p$ tends to zero. Very roughly, the force pulling each chromosome toward the equator of the half-spindle is given by

$$f = 2\,\frac{\gamma_e - \gamma_p}{l}\,s\,, \tag{9}$$

where l is the length of the half-spindle, and s the area of the cross-section of the chromosome.

The quantity $\gamma_e - \gamma_p$ is a function of disorientation, and therefore a function of time. Its theoretical determination should proceed from considerations of the "relaxation time" of the oriented structure. This can again be roughly estimated by considering the angular velocity of thermal rotation of a P molecule. Thus the expression for f in equation (9) will involve the size and mass of the P molecules. Once f is known as a function of time, the speed of the moving chromosomes can be determined approxi-



a *b*

FIGURE 4

mately from considerations of viscous resistance. The viscosity will in this case also decrease as the orientation decreases. The general picture adopted here is not unlike that suggested by Bernal (1940), except that we do not have to make the additional assumption which Bernal makes, namely, that the chromosomes produce a special liquefying substance. Moreover, our formulation is somewhat more quantitative than Bernal's.

The disappearance and reappearance of the nuclear membrane may be connected with the orientation of the P molecules. When the P molecules are not oriented, we may have a structure like the one shown in Figure 4a, where the shorter molecules, forming the membrane, may be oriented on the surface of an isotropic liquid. The radial orientation of the membrane molecules may become impossible when the P molecules are oriented (Fig. 4b), because the whole structure of the field of force changes.

The important feature of the above suggestions is that they assume five *inequalities* (1), (3), (6), (7), and (8). If we know the range of variation of any two quantities x and y, know the mean values $\bar{x}$ and $\bar{y}$, and the stand-

ard deviations σ_x and σ_y of their distributions, we can evaluate the probability of the inequality

$$x > y \,. \tag{10}$$

If $p_1(x)$ and $p_2(y)$ are the distribution functions of x and y, then the probability of (10) is given by

$$p\,(x > y) = \int_0^\infty p_1\,(x) \left\{ \int_0^x p_2\,(y)\, dy \right\} dx \,. \tag{11}$$

The range of variations and the distribution of the quantities involved in our inequalities (1), (3), (6), (7), and (8) can in principle be determined empirically. Therefore, in principle at least, we can calculate the probability of a cell forming by chance in such a way that it will multiply indefinitely by division.

If inequality (1) does not hold, the cell never divides. It will reach asymptotically a size limited by the penetration of metabolites.

If inequality (3) does not hold, then a cell *above* a certain size will not divide. Below a certain size it may divide into the smallest fragments.

If inequality (6) does not hold, there will be no mitosis. If all chromosomes are essential to the life of the cell, a cell dividing with unequal distribution of chromosomes will not survive. The probability of such pathological divisions may be calculated and compared with observed incidences, if any.

Liquefaction or disorientation of the P molecules at early metaphase, before the chromosomes are pulled apart, will arrest mitosis. Presence of small bodies with strong affinity for the ends of P molecules may result in aster-like structures. The mechanism implied in inequality (7) will result in the attraction of chromosomes by re-formed "asters," a phenomenon observed by Pease (1941).

If inequality (1) does not hold, but chromosomes grow without the constituent chains being separated, giant chromosomes would be formed. It would be interesting to see whether some special assumption about the nature of P molecules would lead to such a probability of inequality (1), which coincides with the actual frequency of occurrence of giant chromosomes. The problem undoubtedly will be complicated by considerations of the mechanism of multiplication of the chromosome chains themselves.

As stated in the title, all the above is merely a collection of some suggestions for a theory. Only further research will show whether these suggestions are useful. They definitely outline a number of specific physicomathematical problems which are relevant to cell biophysics. Such phe-

nomena as elongation of freely dividing cells, which are so well described quantitatively by the diffusion drag force theory, will have to be reinterpreted. Some conclusions of the old theory may be carried over directly. Equation (5) thus gives us essentially the size of a dividing nucleus, since complete orientation is a necessary condition for division. Though different from the corresponding expression obtained in the diffusion drag force theory, the similarity is obvious.

If lactic acid is one of the principal sources of hydrogen ions in the cell, and if the latter is the cause of orientation of the P molecules, then the conclusions of the diffusion drag force theory about the role of glycolysis in cell division remain fundamentally unchanged.

In developing a theory along the above outline it will be necessary to take into account the recent cytochemical studies (Caspersson, 1950; Leuchtenberger, 1949; Leuchtenberger and Schrader, 1951; Schrader and Leuchtenberger, 1951) which have important implications in regard to possible mechanisms of cell division.

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ON OPTIMAL ARRANGEMENTS IN SOME SOCIAL LEARNING SITUATIONS

LEO A. GOODMAN*
COMMITTEE ON STATISTICS AND DEPARTMENT OF SOCIOLOGY
THE UNIVERSITY OF CHICAGO

The problem of social learning has been studied by psychologists and sociologists in the laboratory and the real world. We first consider the special, somewhat timely, problem of teaching a group of men to be good paratroopers. Some mathematical models are developed for a simple social learning situation, and necessary and sufficient conditions are then given for obtaining the "best" learning results or "most" learning for these models. The results are then generalized to cover other social learning situations; for example, classroom teaching, possibly.

Let us first consider the group learning situation. If one learning situation A_1 is "better" than the next A_2 we would expect the chance that all the persons will learn to be no less in situation A_1 than the chance that all the persons will learn in situation A_2. We might also expect the chance that no more than one (0 or 1) person will fail to learn will be no less in situation A_1 than in A_2, and the chance that no more than two (0, 1, or 2) persons will fail to learn will be no less in situation A_1 than in A_2, etc.

Now let us consider a group of men whom we want to transform into jumpers. By psychological and psychiatric diagnoses we can determine whether or not person W will be more likely to jump than person V (that is, in the paratrooper terminology, which is less of a quitter). We shall assume that there is a certain initial chance p_w (proneness to jumping) that person W will jump. We shall see later that it will not be required to estimate this probability in practice but only to say how many persons in the group have better chances of jumping than W. We shall say person W is better with respect to action J than person Z if, and only if, $p_w > p_z$.

We expect that the event of seeing others jump may have some effect on a person's proneness to jump. Let $s_j(p)$ denote the chance that a person, whose initial proneness was p, will jump given that he has seen j people

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jump. It seems reasonable to postulate that $s_j(p)$ is a nondecreasing function of p (increasing for some values of p). The quantity $n_j(p) = s_j(p)/s_{j-1}(p)$ is a measure of the relative effect on a person, whose initial proneness was p, of seeing the jth person jump.

Let us consider the hook-up system and corresponding model where, when a man who is hooked up in the airplane refuses to jump, all those men hooked up in line after him are unable to leave the plane. One learning situation A_1 will be defined as "better" than another A_2 if the probability that no more than c persons will fail to jump in situation A_1 is no less than in situation A_2, for $c = 0, 1, 2, \ldots$. We might raise the question as to which is the best (optimal) way of lining up the men in the plane. What is the optimal arrangement of the men in line?

Theorem 1: A. If there exists an optimal arrangement for the model under consideration it can be no better than that obtained by placing the best man in the first position, the next best man second, the third best man third, etc.

B. The arrangement of men from best to worst is the optimal learning situation if and only if $n_j(p)$ is a nonincreasing function of p.

Proof: The chance that at least c will jump in our model equals the chance that the first c will jump. This is, in fact, equal to

$$Pr\{j \geq c\} = s_0(p_0)\, s_1(p_1)\, s_2(p_2) \ldots s_{c-1}(p_{c-1}),$$

where p_i is the initial proneness of the person who is hooked up in the $i+1$ place in line. If $p_i \geq p_j$ for some $i > c-1$ and $j \leq c-1$, then, by the monotonic nature of $s_j(p)$, the total probability $Pr\{j \geq c\}$ will not be decreased if the person with the initial proneness p_i changes position with the person with proneness p_j. Hence, we have proved part A of the theorem.

Now for part B. Let us consider the case A_1 where $p_0 \geq p_1 \geq p_2 \geq \ldots \geq p_{i-1} \geq p_i \geq \ldots$. It will suffice to show that this particular arrangement is better than the arrangement A_2 where persons $i-1$ and i have changed positions (all others remaining in the same position) if, and only if, $n_i(p)$ is a nonincreasing function of p. We have, when $c \geq i$,

$$D = Pr\{j \leq c \mid A_1\} - Pr\{j \leq c \mid A_2\}$$

$$= K\,[s_{i-1}(p_{i-1})\, s_i(p_i) - s_{i-1}(p_i)\, s_i(p_{i-1})],$$

where K is positive. Hence, the difference $D \geq 0$ if, and only if,

$$[s_{i-1}(p_{i-1})\, s_i(p_i) - s_{i-1}(p_i)\, s_i(p_{i-1})] \geq 0$$

or

$$\left\{\frac{s_i(p_i)}{s_{i-1}(p_i)} - \frac{s_i(p_{i-1})}{s_{i-1}(p_{i-1})}\right\} \geq 0.$$

Since $p_i \leq p_{i-1}$, the last condition is equivalent to the condition that $n_i(p)$ is a nonincreasing function of p. *Q.E.D.*

It should be pointed out that in the preceding theorem we had not dealt with the case where $s_{i-1}(p) = 0$ for some values of p. This case causes no real difficulty and requires only slight changes in the wording of *Theorem 1* and the results which will follow.

Theorem 1 is sufficiently general to deal with the paratrooper hook-up system; i.e., where the chance of jumping is zero after there has been a failure in the plane. However, in general social learning situations it is clear that the event of seeing others fail may have some effect on a person's initial proneness to perform an event, but clearly the effect will not be to reduce his chance of performance to zero. Now let $s_{jk}(p)$ denote the chance that person, whose initial proneness was p, will jump given that he has seen j people jump and k people fail to jump. It seems reasonable to postulate that $s_{jk}(p) \geq s_{j-1,\,k+1}(p)$.

We now have the following intuitively clear

Lemma 1: The probability of obtaining at least d further failures given that there have been j jumps and k failures is no greater than the probability of obtaining at least d further failures given that there have been $j - 1$ jumps and $k + 1$ failures.

Proof: For $d = 0$, we have

$$Pr\{f \leq d = 0 \mid j,\ k\} = s_{jk}(p_{j+k})\, s_{j+1,\,k}(p_{j+k+1})\, s_{j+2,\,k}(p_{j+k+2}) \cdots,$$

hence

$$Pr\{f \leq d = 0 \mid j,\ k\} \geq Pr\{f \leq d = 0 \mid j - 1,\ k + 1\}.$$

Now let us consider $d = 1$. The lemma is true when $Pr\{f \leq d \mid j, k\} = P$ is a nondecreasing function of $s_{mn}(p) = s$. We therefore wish to show that $\delta P/\delta s \geq 0$ (we have assumed differentiability of s to simplify the presentation, but this is not a necessary assumption). For $d = 1$, we have

$$P = s_{j,\,k} s_{j+1,\,k} s_{j+2,\,k} \cdots + \sum_{t=j} s_{j,\,k} s_{j+1,\,k} \cdots (1 - s_{t,\,k})\, s_{t,\,k+1} s_{t+1,\,k+1} \cdots$$

and

$$\frac{\delta P}{\delta s_{mn}} = \begin{cases} \displaystyle\sum_{t=j} s_{jk} s_{j+1,\,k} \cdots (1 - s_{t,\,k})\, s_{t,\,k+1} \cdots s_{m-1,\,k+1} s_{m+1,\,k+1} \cdots \\ \qquad \text{when } n = k + 1 \\ s_{jk} s_{j+1,\,k} s_{j+2,\,k} \cdots s_{m-1,\,k} s_{m+1,\,k} s_{m+2,\,k} \cdots \\ - s_{j,\,k} s_{j+1,\,k} s_{j+2,\,k} \cdots s_{m-1,\,k} s_{m,\,k+1} s_{m+1,\,k+1} \\ + \displaystyle\sum_{t=m+1} s_{jk} s_{j+1,\,k} \cdots s_{m-1,\,k} s_{m+1,\,k} \cdots (1 - s_{t,\,k})\, s_{t,\,k+1} s_{t+1,\,k+1} \\ \qquad \text{when } n = k. \end{cases}$$

Hence

$$\frac{\delta P}{\delta s_{m,\,k+1}} \geq 0$$

and

$$\frac{\delta P}{\delta s_{m,\,k}} = K + s_{jk} s_{j+1,\,k} s_{j+2,\,k} \cdots s_{m-1,\,k} [\, s_{m+1,\,k} s_{m+2,\,k} \cdots - s_{m,\,k+1} s_{m+1,\,k+1} \cdots]$$

where K is non-negative. We also have that

$$\frac{\delta P}{\delta s_{m,\,k}} \geq 0$$

since $[s_{m+1,\,k} s_{m+2,\,k} \cdots - s_{m,\,k+1} s_{m+1,\,k+1} \cdots] \geq 0$ by the preceding result for $d = 0$. We may now proceed to prove the lemma in this way by mathematical induction on d. *Q.E.D.*

In analogy to the hook-up model, we define

$$n_{jk}(p) = \frac{s_{j,\,k}(p)}{s_{j-1,\,k}(p)} \qquad \text{and} \qquad q_{jk}(p) = \frac{f_{j,\,k}(p)}{f_{j,\,k+1}(p)},$$

where $f_{j,\,k} = 1 - s_{j,\,k}$. We have

Theorem 2: The arrangement of men from best to worst is the optimal arrangement if $n_{jk}(p)$ and $q_{jk}(p)$ are nonincreasing functions of p.

Proof: Let us consider the case A_1 where $p_0 \geq p_1 \geq p_2 \geq \ldots \geq p_{i-1} \geq p_i \geq \ldots$. It will suffice to show that this particular arrangement is better than the arrangement A_2 where persons $i - 1$ and i have changed positions (all others remaining in the same position). If j jumps and $i - j - 1$ failures have been observed by the person in the ith position, the possible results for the ith and $i + 1$st person have the following probabilities for case A_1:

$$\{0\}_1 = s_{j,\,i-j-1}(p_{i-1})\, s_{j+1,\,i-j-1}(p_i)$$

$$\{1\}_1 = s_{j,\,i-j-1}(p_{i-1})\, f_{j+1,\,i-j-1}(p_i) + f_{j,\,i-j-1}(p_{i-1})\, s_{j,\,i-j}(p_i)$$

$$\{2\}_1 = f_{j,\,i-j-1}(p_{i-1})\, f_{j,\,i-j}(p_i).$$

If we now consider case A_2, where the p_i and p_{i-1} are interchanged, and then subtract the probabilities obtained, we have

$$\{0\}_1 - \{0\}_2 = s_{j,\,i-j-1}(p_{i-1})\, s_{j+1,\,i-j-1}(p_i) - s_{j,\,i-j-1}(p_i)\, s_{j+1,\,i-j-1}(p_{i-1})$$

$$= \{n_{j+1,\,i-j-1}(p_i) - n_{j+1,\,i-j-1}(p_{i-1})\}\, K \geq 0$$

and

$$\{2\}_2 - \{2\}_1 = f_{j,\, i-j-1}(p_i)\, f_{j,\, i-j}(p_{i-i}) - f_{j,\, i-j-1}(p_{i-1})\, f_{j,\, i-j}(p_i)$$
$$= \{q_{j,\, i-j-1}(p_i) - q_{j,\, i-j-1}(p_{i-1})\}M \geq 0 .$$

Since

$$\sum_{t=0}^{2} \{t\}_1 = \sum_{t=0}^{2} \{t\}_2 = 1 ,$$

we have

$$\sum_{t=0}^{2} [\{t\}_1 - \{t\}_2] = 0$$

and, therefore,

$$\sum_{t=0}^{1} [\{t\}_1 - \{t\}_2] \geq 0 .$$

We write $\{0\}_1 - \{0\}_2 = d_0(j,\ i-j-1)$ and $\{2\}_2 - \{2\}_1 = d_2(j, i-j-1)$. We have then $\{1\}_1 - \{1\}_2 = d_2(j, i-j-1) - d_0(j, i-j-1)$.

Now let us consider the probability P_0 that all will jump. There is no difference for this case between the hook-up model of *Theorem 1* or the present model. Hence, it is clear that the probability that all will jump is no less for A_1 than A_2. We have, in fact, that the difference between P_0 for arrangement A_1 and P_0 for arrangement A_2 is $\Delta P_0 = (0) \cdot d_0(i-1, 0) \cdot [0, 0]$, where (k) is the probability that there will be k failures among the persons who perform before person $i-1$, and $[k, t]$ is the probability that there will be t failures among the persons who are to perform after person i, given that there have been a total of k failures among the persons $0, 1, 2, \ldots, i-1, i$.

We are now ready to consider the probability P_1 that one will fail to jump. We may differentiate three cases as follows: the failure occurring before person $i-1$, after person i, or by either person $i-1$ or i. Hence we have

$$\Delta P_1 = (0) \cdot d_0(i-1, 0) \cdot [0, 1] + (0) \cdot [d_2(i-1, 0) - d_0(i-1, 0)] \cdot [1, 0] + (1) \cdot d_0(i-2, 1) \cdot [1, 0],$$

and

$$\Delta P_0 + \Delta P_1 = (0) \cdot d_0(i-1, 0) \cdot \{[0, 0] + [0, 1] - [1, 0]\} + (0) \cdot d_2(i-1, 0) \cdot [1, 0] + (1) \cdot d_0(i-2, 1) \cdot [1, 0].$$

From *Lemma 1* we have that $[0, 0] \geq [1, 0]$, and, therefore, $\Delta P_0 + \Delta P_1 \geq 0$.

Now let us consider the probability P_2 that two will fail to jump. We have

$$\begin{aligned}\Delta P_2 = {} & (0) \cdot d_0(i-1, 0) \cdot [0, 2] + (0) \cdot [d_2(i-1, 0) \\ & - d_0(i-1, 0)] \cdot [1, 1] + (1) \cdot d_0(i-2, 1) \cdot [1, 1] \\ & - (0) \cdot d_2(i-1, 0) \cdot [2, 0] + (1) \cdot [d_2(i-2, 1) \\ & - d_0(i-2, 1)] \cdot [2, 0] + (2) \cdot d_0(i-3, 2) \cdot [2, 0]\end{aligned}$$

and

$$\begin{aligned}\Delta P_0 + \Delta P_1 + \Delta P_2 = {} & (0) \cdot d_0(i-1, 0) \cdot \{[0, 0] + [0, 1] + [0, 2] \\ & - [1, 0] - [1, 1]\} + (0) \cdot d_2(i-1, 0) \cdot \{[1, 0] + [1, 1] - [2, 0]\} \\ & + (1) \cdot d_0(i-2, 1) \cdot \{[1, 0] + [1, 1] - [2, 0]\} \\ & + (1) \cdot d_2(i-2, 1) \cdot [2, 0] + (2) \cdot d_0(i-3, 2) \cdot [2, 0].\end{aligned}$$

We may now proceed to prove the theorem in this way by mathematical induction on the number of failures. *Q.E.D.*

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NOTE ON THE GROWTH OF BACTERIAL POPULATIONS

A. T. Reid*
Committee on Mathematical Biology
The University of Chicago

In this note the explicit solution is given to an equation, suggested by C. N. Hinshelwood (1946), describing the growth of a bacterial population under the assumption that toxic products are a limiting factor. The behavior of the culture as a function of time and the parameters (initial number, rate of growth, and rate of production of toxic substance) is discussed.

C. N. Hinshelwood (1946) in his studies on bacterial growth processes has considered the relation between the number of organisms in the culture and the concentration of some toxic metabolic product. Hinshelwood's equation, which states that the number of organisms will increase at a rate proportional to the number at any time and decrease at a rate (per organism) proportional to the concentration of the toxic substance, is as follows:

$$\frac{dn}{dt} = kn\,(1 - a\,c)\,; \tag{1}$$

where n is the number of organisms in the culture, c is the concentration of the toxic metabolic products, and k and a are positive constants. If the toxic substance is formed at a rate r per organism, we have

$$\frac{dc}{dt} = rn$$

or

$$c = r\int_0^t n\,dt\,. \tag{2}$$

We can now write (1) as

$$\frac{dn}{dt} = kn\left(1 - ar\int_0^t n\,dt\right). \tag{3}$$

The purpose of this note is to obtain an explicit solution for $n(t)$ and discuss its behavior as a function of the parameters.

* Public Health Service Research Fellow of the National Cancer Institute, National Institutes of Health, Federal Security Agency.

To solve the integrodifferential equation (3) we divide both sides by n and make the substitution $y = \ln n$ or $n = e^y$. We have now for (3)

$$\frac{dy}{dt} = k - ak\int_0^t e^y dt .$$

Differentiating with respect to t, we obtain

$$\frac{d^2y}{dt^2} = -ake^y . \tag{4}$$

We have put $a = ar$ in (4). Multiplying (4) by $2dy/dt$ and integrating, we have

$$\left(\frac{dy}{dt}\right)^2 = -2ake^y + C ,$$

where $C = k^2 + 2akn_0$, since $n = n_0$ and $dy/dt = k$ when $t = 0$. Now

$$\frac{dy}{dt} = \pm\sqrt{k^2 + 2ak(n_0 - e^y)} . \tag{5}$$

Expressing (5) in terms of n we have

$$\frac{1}{n}\frac{dn}{dt} = \pm\sqrt{k^2 + 2ak(n_0 - n)} . \tag{6}$$

Thus for the range of n where dn/dt is positive

$$t = \int_{n_0}^{n} \frac{dn}{n\sqrt{k^2 + 2ak(n_0 - n)}} . \tag{7}$$

Performing the integration we have

$$t = \frac{1}{A}\ln\left[\frac{(\sqrt{A^2 - 2akn} - A)}{(\sqrt{A^2 - 2akn} + A)} \cdot \frac{(k + A)}{(k - A)}\right], \tag{8}$$

or, solving for $n(t)$,

$$n(t) = \frac{Ce^{At}}{(1 - Be^{At})^2} . \tag{9}$$

In the above we have put

$$A = \sqrt{k^2 + 2akn_0} ,$$

$$B = \frac{k - A}{k + A} ,$$

and

$$C = -\frac{2A^2B}{ak}.$$

We begin the study of the behavior of $n(t)$ by differentiating (9) to obtain

$$\frac{dn}{dt} = AC\,e^{At}(1 - B\,e^{At})^{-2} + 2ABC\,e^{2At}(1 - B\,e^{At})^{-3}.$$

Setting the derivative equal to zero and solving for t, we obtain

$$t^* = \frac{1}{A}\ln\left(-\frac{1}{B}\right) = \frac{1}{A}\ln\left(-\frac{k+A}{k-A}\right). \tag{10}$$

Differentiating again and introducing t^* for t, we find that the second derivative is less than zero. Hence $n(t)$ has its maximum value when t

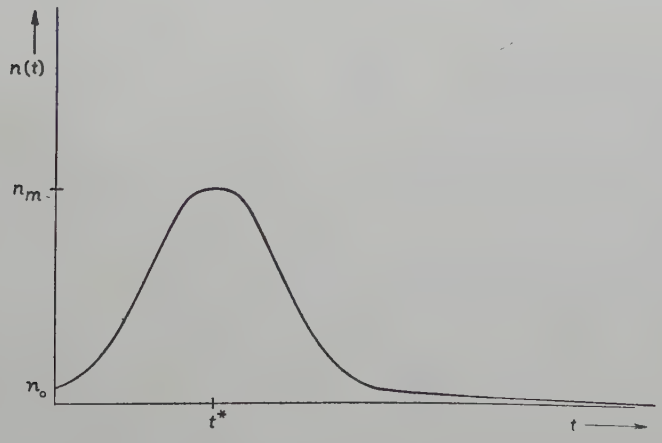

FIGURE 1

assumes the value given by (10). By introducing t^* in (9), we find the maximum number of organisms to be

$$n_m = n_0 + \frac{k}{2a}. \tag{11}$$

In (10) we have the time required for the population to reach its maximum value as a function of the initial number of organisms, and in (11) we give the maximum number of organisms as a function of the initial number.

Beyond the maximum point dn/dt is negative, and a completely analogous calculation shows the growth curve to be symmetrical with respect to the line $t = t^*$. The complete growth curve is shown in Figure 1.

It is of interest to point out that (9) can be considered as a modification of the well-known logistic equation which occurs in many population studies. The distinguishing feature of our equation is that the denominator is squared, while in the logistic equation it is not. Moreover, in the logistic equation $B = -C$.

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MATHEMATICAL BIOPHYSICS OF COLOR VISION

H. D. LANDAHL
COMMITTEE ON MATHEMATICAL BIOLOGY
THE UNIVERSITY OF CHICAGO

A neural mechanism is studied in which three primary receptors interact in such a manner that only a small region is in activity for a given colored stimulus. The similarity to the color triangle is noted. The introduction of an additional primary receptor may or may not change the dimensionality of sensation space in this mechanism. Problems of discrimination of color, absolute judgment of saturation, and hue are discussed.

It is the purpose of the present paper to develop some aspects of a neural mechanism which were introduced to represent some qualitative features of color vision (Householder and Landahl, 1944). It was assumed that there are three types of primary receptors, responding differently to various wave lengths λ of light, in such a manner as to cover the visible range. Let $p_i(\lambda)$ be a measure of the response of the ith receptor to a unit intensity of wave length λ. For a given light stimulus with an energy spectrum $S(\lambda)$ let there result a stimulus of intensity

$$S_1 = \int S(\lambda)\, p_1(\lambda)\, d\lambda$$

in the first type of receptors. The stimulus intensities S_2 and S_3 of the other type receptors are similarly defined. To a given $S(\lambda)$ there is therefore a corresponding excitation pattern which we may denote by (S_1, S_2, S_3), or, more simply, by (S_i).

Let each receptor of type i be connected to neural elements lying in a plane C defined by three points C_1, C_2, C_3. We consider the region C to be a plane for convenience only. Let the number of neural elements in C be large enough so that we may speak of their density per unit area, and, similarly, let the number of connections from the type i receptors be large. We now define $\rho_i(x, y)$ as the density of connections from type i receptors to some point (x, y) in C. For convenience let C_1, C_2, and C_3 be equidistant from each other, the center of the triangle $C_1C_2C_3$ being the origin $(0, 0)$. Let the x-axis be taken in the direction of C_1, the units being chosen

such that C_1 is at (1, 0) and thus C_2 is at $(-\frac{1}{2}, \cos 30°)$ and C_3 at $(-\frac{1}{2}, -\cos 30°)$.

We shall now suppose that each of the density functions $\rho_i(x, y)$ depends only upon the distance d_i from the point (x, y) to the corresponding C_i, i.e., $\rho_i(x, y) = \sigma_i(d_i)$, and that $\sigma(d)$ is a monotonic decreasing function. It might be supposed that $\sigma(d)$ is a normal error distribution due to some random process in development and that since we shall only be interested in values of d which are small, so that if $\sigma_0 i$ and γ_i are constants, $\sigma_i(d_i)$ is given by

$$\sigma_i(d_i) = (1 - \gamma_i d_i^2)\, \sigma_{0i} . \tag{1}$$

It can be shown that the replacement of d_i^2 by $|d_i|$ leads to similar results.

The intensity of excitation E_i (Rashevsky, 1948) is a function of the intensity S_i. We shall consider two cases, one in which the relation is linear and the other in which it is logarithmic in the external intensity S_i. Thus in the first case we have, if h_i is the threshold,

$$E_i = a_i (S_i - h_i) . \tag{2}$$

If we consider only the steady state, then the density of the excitation factor ϵ_i at any point (x, y) due to E_i is given by $E_i \sigma_i$ so that we have

$$\epsilon_i = E_i \sigma_i = d_i \sigma_{0i} (S_i - h_i)(1 - \gamma d_i^2) \tag{3}$$

and, hence, if we define

$$S_i' = a_i \sigma_{0i} (S_i - h_i) = E_i \sigma_{0i} , \tag{4}$$

the total excitation density $\epsilon(x, y)$ is given by

$$\epsilon(x, y) = \epsilon_1 + \epsilon_2 + \epsilon_3 = S_1' + S_2' + S_3' - \gamma_1 S_1' d_1^2 - \gamma_2 S_2' d_2^2 - \gamma_3 S_3' d_3^2 . \tag{5}$$

If the γ's are about equal and not too large, $\epsilon(x, y)$ is a function having a maximum value within the triangle $C_1 C_2 C_3$. Suppose now that the region C is connected with another region C' by excitatory pathways, in such a way that there is a point to point correspondence between the two regions, preserving the geometry. Let there also be numerous cross-inhibitory paths from each connection in C to every pathway originating in C', which thus tend to restrict the excitation in the region C' to those elements in the neighborhood of the point P' of C' corresponding to the P of C for which $\epsilon(x, y)$ is a maximum (Rashevsky, 1948, p. 377). Thus for a particular $S(\lambda)$ only a certain region in C' will be excited and the position of this region will depend upon $S(\lambda)$, i.e., the relative amounts of energies

of the different wave lengths of the incoming light. Any $S(\lambda)$ giving the same values for S_1, S_2, and S_3 results in the same region being excited.

We may solve for the coordinates of the center of the region as a function of S_1, S_2 and S_3 by setting $\partial\epsilon/\partial x = \partial\epsilon/\partial y = 0$, and thus obtain

$$x^* = \frac{2\gamma_1 S_1' - \gamma_2 S_2' - \gamma_3 S_3'}{2(\gamma_1 S_1' + \gamma_2 S_2' + \gamma_3 S_3')}, \tag{6}$$

$$y^* = \frac{\sqrt{3}(\gamma_2 S_2' - \gamma_3 S_3')}{2(\gamma_1 S_1' + \gamma_2 S_2' + \gamma_3 S_3')}. \tag{7}$$

If we set $X^* = x^*$, $Y^* = y^*\sqrt{\frac{3}{2}} - x^*/3$, $Z^* = -x^*/2 - \sqrt{3}y^*/2$, X, Y, and Z become the coordinates of a point in the coordinate system OC_1, OC_2, OC_3. Note that $X + Y + Z = 0$ and Y and Z can be obtained from equation (6) by cyclic permutation of the subscripts. The point C_1 can be represented by $(1, -\frac{1}{2}, -\frac{1}{2})$, C_2 by $(-\frac{1}{2}, 1, -\frac{1}{2})$, and C_3 by $(-\frac{1}{2}, -\frac{1}{2}, 1)$. If now $\gamma_1 S_1' \gg \gamma_2 S_2'$ and $\gamma_3 S_3'$, then $X = 1$, $Y = Z = -\frac{1}{2}$, so that only those neurons in the region about C_1', corresponding to C_1, are active. From symmetry it can be seen that if $\gamma_2 S_2' \gg \gamma_1 S_1'$, $\gamma_3 S_3'$, only neurons about C_2' are active. On the other hand, if $\gamma_1 S_1' \sim \gamma_2 S_2' \gg \gamma_3 S_3'$, the active region in C' lies near the line between C_1' and C_2', while if $\gamma_1 S_1' = \gamma_2 S_2' = \gamma_3 S_3'$, the active region of C' is at the center of the triangle formed by C_1', C_2', and C_3'. Note that for any value θ, if all θS_i and S_i are far above threshold, the stimulus with an excitation pattern $(\theta S_1, \theta S_2, \theta S_3)$ results in an excitation with a maximum in almost exactly the same position in C' as does (S_1, S_2, S_3). But if any S_i or θS_i is near h_i, a general change in intensity by a factor θ changes the position in C' by an amount which depends upon the relative values of the h_i. Furthermore, if $S_i \gg h_i$ for each i, and if $(S_i) \equiv (S_1, S_2, S_3)$, the center of the region which corresponds to the stimulus $(S_i + \theta/\alpha_i\sigma_{0i}\gamma_i)$ is always nearer to the origin than the point which corresponds to (S_i), the point corresponding to $(S_i + \theta/\alpha_i\sigma_{0i}\gamma_i)$ being at the origin if θ is large enough.

If $S_1' = S_2' = S_3'$, and $S_i \gg h_i$, the intensities ϵ_1, ϵ_2, and ϵ_3 at C_1, C_2, and C_3 respectively are equal. Also if $\gamma_1 = \gamma_2 = \gamma_3$, these physiologically equal values for the ϵ_i result in an excitation about the origin of C'. If the distributions σ_i are the result of the same random process we might expect this would be so and $\gamma_i = \gamma_j$; also $\sigma_{0i} = \sigma_{0j}$. In most of the following we shall make this an assumption and thus drop the subscript $_i$ of σ_{0i} and γ_i.

From the above discussion it can be seen that we have mapped the familiar color triangle (cf. Wright and Martin, 1946) on to the neural

region C'. Energies impinging upon three distinct receptors result in a response somewhere in a plane region, the position depending upon the relative amounts of energy in the three components. The primaries themselves have no special properties, and a mixture of any two does not possess any special properties of either.

A change in $S(\lambda)$, which causes the corresponding point P' (in C') to move radially, corresponds to no change in hue. This type of constancy can be taken into account by the following addition to the mechanism. Let there be neuronal elements lying along some closed curve C_H containing the triangle $C_1C_2C_3$. Let each neuron of C_H have dendritic connections with the axon endings of those neurons of C' in such a way that connections are made only radially toward the origin O' of C' and in such a manner that the probability of a connection decreases to zero as the origin is approached. Then the neurons in the same neighborhood of C_H are excited when there is no change in hue, the excitation being greater, however, for a more saturated color. The assumption that the connections of the neurons in a small neighborhood of some point of C_H be made almost exactly radially is not at all necessary. There can be a very considerable lateral spread and even a spread past the origin if C_H transmits through to another C'_H only in the region of maximum excitation. Such a radial structure as that of the center C_H requires only a simple tropism for its development.

In a similar manner, a center C_S, in which the neurons in a linear array each receive impulses from different annular regions, would result in a response which would depend almost entirely upon the degree of saturation. Such a structure could arise as a result of the various elements of C_S being attracted, during development, to various absolute concentrations of some substance produced at the origin of C' which then diffuses outward. Thus C_S is a much less probable structure than C_H. It may be noted that absolute judgments of saturation are relatively poor compared with judgments of hue.

We shall next determine the size and shape of a region in C' which becomes active for a given $S(\lambda)$. Two colored stimuli producing excitation in regions which just fail to touch should correspond to two stimuli which are just clearly distinguished. Thus the radius R of the active region in C' would be a suitable measure of the psychological distance between two colored stimuli. The radius R is small where the discrimination is fine. Suppose then that transmission from C to C' occurs for values of ϵ within an interval $\epsilon_{max} \geq \epsilon \geq \epsilon_{max} - \Delta\epsilon$ and the range $\Delta\epsilon$ is nearly independent of the total intensity of illumination. Then, since the radius of curvature

of $\epsilon(x, y)$ can be shown to be constant, we find the radius R of the active region of C' to be given by

$$R = \sqrt{\frac{\Delta\epsilon}{\gamma\,(S_1' + S_2' + S_3')}}, \tag{8}$$

so that accuracy of discrimination increases slowly with illumination. For not too large distances, points on the triangle C_1', C_2', C_3' which are equally distant are distinguished with equal difficulty.

If, however, one uses a secondary set of "primaries," the circles implied by (8) will become ellipses. Furthermore, if one plots a circle in the C' plane, the result is an ellipse in the plane $f_i f_j$ where f_i is defined by

$$f_i = \frac{a_i \gamma_i\,(S_i - h_i)\,\sigma_{0i}}{\Sigma a_j \gamma_j\,(S_j - h_j)\,\sigma_{0j}}.$$

If $S_i \gg h_i$ for each i, the quantity f_i becomes the fraction of energy going to i in arbitrary units. In this case a pair of f's may be chosen as coordinates, the results of any plot depending upon which pair is chosen. A plot of this kind is conventionally used, and it is on such a plot that the data yield ellipses (cf. Brown, 1951). If one considers the more likely possibility that the points C_1, C_2, and C_3 are not exactly equidistant, the result is further complicated.

In the above case we have assumed E_i to be linear in S_i. This is generally not the case for visual phenomena. It is more often assumed, as a result of various observations, that the relation is logarithmic. We shall now consider the effect of this complication. Instead of equation (2), we will now have, if β_i is a constant,

$$E_i = \beta_i \log \frac{S_i}{h_i}. \tag{9}$$

If no further changes are made, we find that in this case the active region of C' changes its position slowly with change of intensity, the proportions of the S_i being unchanged. Generally the change is such that at higher intensities the position of the active region is nearer to the origin. The change appears to be too rapid to correspond to the actual situation (cf. Brown, 1951). We shall therefore consider another mechanism.

Let each primary receptor produce an amount j of inhibitory factor (instead of excitatory) at a connection A_i along the pathway to C. Let there also be excitatory elements which react to the total physiological intensity $(S_1/h_1 + S_2/h_2 + S_3/h_3)$ and which act at each of the connections A_i along the pathways between the receptors and C. Then the

amount of excitation ϵ_i at A_i will be the quantity $\beta' \log (S_1/h_1 + S_2/h_2 + S_3/h_3)/h' - \beta \log S_1/h_1$. Then ϵ will be given by the following expression, instead of by (3),

$$\epsilon(x, q) = \sum_{i=1}^{3} (\sigma_{0i} - \sigma_{0i}\gamma_i d_i^2) \left[\beta' \log \frac{\frac{S_1}{h_1} + \frac{S_2}{h_2} + \frac{S_3}{h_3}}{h'} - \beta \log \frac{S_i}{h_i} \right], \quad (10)$$

the d_i's being the same distances as in equation (5) and thus being functions of x and y. If we simplify matters by assuming $h' = 1$, $\beta_i = \beta'$, $\gamma_i\sigma_{0i} = \gamma_j\sigma_{0j}$, and introducing the fractions $f_i = S_i(S_1/h_1 + S_2/h_2 + S_3/h_3)h_i$, so that $f_1 + f_2 + f_3 = 1$, then we find the position of the maximum for any S_1, S_2, S_3 to be given by

$$x = \frac{\log \frac{f_2 f_3}{f_1^2}}{2 \log \frac{1}{f_1 f_2 f_3}}, \quad (11)$$

with similar expressions for Y and Z obtained by permuting the subscripts. In this case, the position does not depend upon the level of the intensity but depends only upon the relative intensities of the components. If $f_1 \approx 1$ or $S_1 \gg S_2$, S_3, then $X \approx -\frac{1}{2}$ and $Y = Z = -\frac{1}{4}$; while if $f_1 \approx 0 (S_1 \gg S_2, S_3)$, $X \approx 1$ and $Y = Z = -\frac{1}{2}$. Thus the representation is inverted with respect to the linear case. The radius of curvature in this case, instead of being given by (8), is a constant, independent of x, y, and S_i.

To study the differences between the two cases corresponding to equations (6) and (11), we may (since in each case the radius of curvature is independent of x, y) compare the effects of changing the relative value of one of the primaries, e.g., f_1. Consider a change such that $f_2 = f_3$; then form the expression $\Delta f_1/\Delta x^*$. This expression shows how great a change in f_1 is required to produce a given change in x subject to the condition that $f_2 = f_3$. For the first case (linear, A, Fig. 1) this ratio is found to be equal to $\frac{2}{3}$ if f_i is defined by

$$f_i = \frac{a_i (S_i - h_i)}{\Sigma a_j (S_j - h_j)}.$$

In the second case, corresponding to equation (11), we find (B, Fig. 1)

$$\frac{\Delta f_1}{\Delta x^*} = \frac{1}{3} \frac{f_1 (1 - f) [\log f_1 + 2 \log (1 - f_1) - \log 4]^2}{(1 - f_1) \log 2 - f_1 \log f_1 - (1 - f_1) \log (1 - f_1)}. \quad (12)$$

In a similar way we can obtain the change Δy^* in y^* when f_2 and $f_3 = f_2$ are changed to $f_2 + \Delta f_2$ and $f_3 - \Delta f_2$. We then find $\Delta f_2/\Delta y^* = 1/\sqrt{3}$ in the linear case (C, Fig. 1) while in the second case (D, Fig. 1) we obtain

$$\frac{\Delta f_2}{\Delta y^*} = \frac{(1 - f_1)}{2\sqrt{3}} [\log f_1 + 2 \log (1 - f_1) - 2 \log 2]. \qquad (13)$$

The signs are reversed in the curves of Figure 1 for the case corresponding to equation (11), since, as was pointed out above, the representation

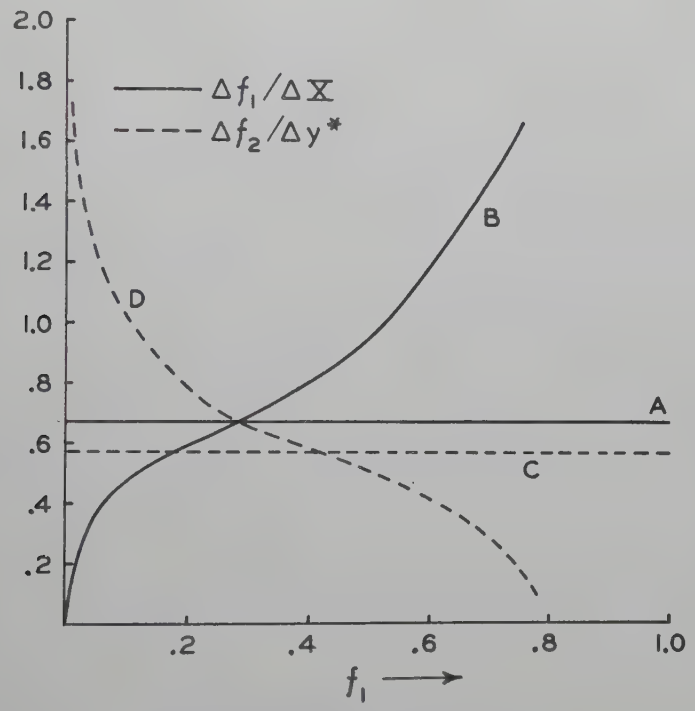

FIGURE 1

in this case is inverted with respect to the first case. In the first case the change in x and y directions are nearly alike and are constant. In the second case a primary and its contrasting color are dissimilar. A small addition of a contrasting color $\Delta(1 - f_1)$ to a large amount of a primary ($f \approx 1$) is relatively ineffective in producing a noticeable change in response (cf. solid curve for $f \approx 1$ in Fig. 1). On the other hand, only a small amount of a primary Δf_1 added to a contrasting color ($f_2 = f_3 \gg f_1$) is necessary to produce a change in the response (solid curve for $f_1 \approx 0$).

We shall now study some effects which might arise if more than three

primaries are involved. We shall only study the simpler linear case as this illustrates the effect of the introduction of additional receptors.

Let there be four kinds of primary receptors which send out pathways into the region C in a manner similar to that considered in the first case above. First suppose these pathways spread out from four points $C_1, \ldots C_4$ which are the corners of the square $C_1C_2C_3C_4$. Let the distribution functions of the densities of connections σ_i be given as above by equation (1). We can then find the point of maximum activity as above, the result being

$$X = x = \frac{S_1 - S_3}{S_1 + S_2 + S_3 + S_4}$$

with expressions for Y, Z, and W obtained by permuting the subscripts. However, since the points lie in a plane, mixtures of only three stimuli can be made equivalent to any compound stimulus which lies within the triangle formed by the three stimuli. Thus from the data on mixture of colors alone, the representation by three "primaries" would be adequate.

If this case were "normal," then an abnormal case arising as a result of the absence of one of the primaries (or its failure to act at C or its acting uniformly over C) would appear to be almost normal so far as color mixture is concerned. However, in the case of three primaries, a complete loss of one would radically change the response to color mixtures. In this case all colors would be arranged along a line. Note that with a partial malfunction of one of the primaries it is possible for the representation to be well spread out over an area or to be essentially a linear arrangement or any intermediate situation.

Now if there are four primaries, but the structure is such that the points $C_1, \ldots C_4$ are not coplanar but, for example, form a regular tetrahedron, then we find

$$X = \frac{(3S_1 - S_2 - S_3 - S_4)}{3\,(S_1 + S_2 + S_3 + S_4)},$$

with similar expressions for Y, Z, and W. In this case it is evident that a color match would require the mixture of four colors in general.

If the functions $p_i(\lambda)$ are such that, for a moderately high intensity, $S_i > h_i$, $i = 1, 2, 3$ regardless of $S(\lambda)$, then there is a band of value near the border of the region C' which would not normally become excited. The points in this border region would correspond to highly saturated colors. For example, if a particular $S(\lambda)$, with given total intensity, results in S_1/S_2 having a maximum for $S_2 = S_3 > h_2 = h_3$, then $x \leq (S_1 - S_2)/(S_1 + 2S_2) = x^* < 1$ and no color can produce excitation at a point

$x > x^*$. However, if the receptors of type 2 and 3 are partially or completely inhibited in any manner, then the result is the activity in the region about $x > x^*$. This inhibition might arise as the result of accommodation to a color $S_2 \approx S_3 \gg S_1$ or due to inhibition from an adjacent region in which $S_2 = S_3 \gg S_1$, provided that the cross-inhibitory effect results in a uniform reduction in all S_i's or S_i in region I inhibits only S_1 in region II, and conversely. In any such situation one might expect to obtain colors appearing to be more saturated than would otherwise be obtained.

It may be noted that in the case of three primary receptors, the intensity can be included so that the result is a color pyramid (Householder and Landahl, 1945). On the other hand, the intensity may be given independently. The results of experiments on color discrimination will be different in these two cases, the representation of intensity having similar geometric properties to color in the first case, while having different properties in the latter. A careful comparison with experimental data may show one arrangement to be a better model than the other. Available data (Brown, 1951) do not appear to be adequate to shed light on this point.

At high enough intensities, the functions E_i must physiologically be bounded so in either case, when the approximations (2) or (9) break down, the active region in C′ will, regardless of the stimulus, move in toward some point located not far from the center.

In most of the above discussion we have considered three groups of receptors, those in each group being considered to be identical. It can be shown that to account for most of the observed data on reaction to color it is only necessary that there be three groups of receptors with the proper geometrical connections, but each having average functions $p(\lambda)$ sufficiently distinct.

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SOME CONTRIBUTIONS TO THE MATHEMATICAL BIOLOGY OF BLOOD CIRCULATION. REFLECTIONS OF PRESSURE WAVES IN THE ARTERIAL SYSTEM

GEORGE KARREMAN
COMMITTEE ON MATHEMATICAL BIOLOGY
THE UNIVERSITY OF CHICAGO

If, along the length of a blood vessel, there is a discontinuous change of diameter, the pressure waves will be reflected at the discontinuity. The transmission and reflection coefficients of the waves are calculated in terms of the ratio of the diameters and the ratio of the propagation velocities of the waves in the parts of the blood vessel. We obtain also the reflection coefficient in terms of the ratios of the diameters, of the elasticity moduli, and of the wall thicknesses.

The possible clinical importance of the results is pointed out for cases of coarctation, arteriosclerosis, and other pathological conditions which might effect local changes in the structure of the blood vessel wall.

Whereas the propagation of pressure waves in a fluid within an elastic tube has already been studied (see Boulanger, 1913; Witzig, 1914), their reflection has not been studied so extensively. W. F. Hamilton and P. Dow (1938) claim to have obtained experimental evidence for the existence of standing waves of the blood pressure in the aorta. In another work Hamilton (1944) has shown that general vasodilatation due to the injection of acetylcholine caused the reflected waves to become weaker. With larger doses of acetylcholine the standing waves were eliminated from all arteries. That the drug had not affected a change in the arterial wall which prevented the transmission of the reflected waves was shown by the fact that these waves reappeared when the leg was grasped tightly at the knee producing a vasoconstriction. This, together with the observation that they also could be brought back by intra-arterial injections of epinephrine in small doses producing vasoconstriction of the dilated arterioles, strongly suggests that the change in radius of the arterioles plays an important role in the production of the reflected waves. This is shown in the purest form by I. G. Porjé (1946), who concludes that in cases of patients with a coarctation (isthmus stenosis) some of the waves are reflected more powerfully than in normal individuals. Porjé also emphasizes the importance of a theoretical study of reflections of pressure waves in the arterial system.

The lack of a theory which includes the study of the reflection relations of the wave has been, in his opinion, the great obstacle in the study of the pulse wave. A similar opinion was expressed some years ago by A. Apéria (1940), whom Porjé quotes. The presence or absence of the reflection of pressure waves gives some indication of the cause of a low blood pressure and the degree of vasodilatation in that condition (Hamilton, 1944). If the blood pressure falls due to a hemorrhage, the arterioles constrict and there will be strongly reflected waves. However, if the blood pressure is low because of dilatation of the peripheral arterioles, reflected waves are absent. The evidence given above suggests that a change in the diameter of the

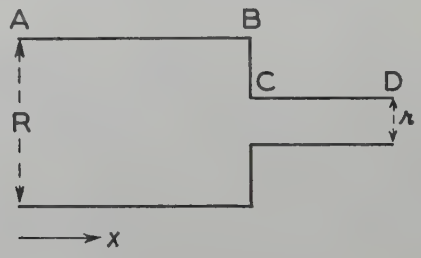

FIGURE 1

blood vessels probably plays an important role as far as the reflection of pressure waves in that vessel is concerned. Therefore, we will investigate theoretically the simplest possible model—directly suggested by the coarctation studies mentioned above—that of a discontinuous change in the diameter of the vessel (Fig. 1).

As at any discontinuity a pressure wave traveling from A to B is partially reflected at the sudden change BC and partially transmitted. To derive expressions for the reflection and transmission coefficients we have to take into account the two conditions (Rayleigh, 1896, p. 63):

$$p_B = p_C \,, \tag{1}$$

the continuity of the pressure, and

$$\pi R^2 v_B = \pi r^2 v_C \,, \tag{2}$$

the continuity of the mass flow, v representing the velocity.

Actually, instead of (1), the Bernouilli equation should be used, but, by taking into consideration that the velocity heads are negligible compared with the pressure heads, (1) results.

Any pressure wave traveling without deformation with velocity c from A to B can be described by

$$p = F\left(t - \frac{x}{c}\right), \tag{3}$$

where t represents the time, x the abscissa measured from an arbitrary origin, as, e.g., A, and F denotes a symbol for a function of the argument $t - x/c$. It can be easily seen that this is the case. Consider a pressure disturbance, or, what amounts to the same thing in elastic tubes, a wall disturbance traveling with velocity c to the right. Suppose at $t = 0$ it is at $x = 0$, so that

$$t - \frac{x}{c} = 0 .$$

Corresponding to (3) the pressure at $x = 0$, when $t = 0$, is then $p = F(0)$. At the time t the disturbance traveling with velocity c is then at $x = ct$. Therefore, that same pressure $F(0)$ is at t at $x = ct$, and then, because

$$t - \frac{x}{c} = 0 ,$$

we have, according to (3), $p = F(0)$ which proves our statement above.

A wave traveling in the direction of the negative x-axis, that is, from B to A, can be correspondingly represented either by

$$p = f\left(t - \frac{x}{-c}\right),$$

because the velocity is then $-c$ instead of c, or by

$$p = f\left(t + \frac{x}{c}\right). \tag{4}$$

Let us assume now that a pressure wave represented by (3) is partially reflected at the discontinuity BC producing a reflected wave represented by (4) and a transmitted wave which, similar to (3), may be represented by

$$p = g\left(t - \frac{x}{c'}\right), \tag{5}$$

the velocity c' in the tube CD being usually different from the velocity c in AB. The total pressure in AB is then the sum of the pressures given in (3) and (4):

$$p_{AB} = F\left(t - \frac{x}{c}\right) + f\left(t + \frac{x}{c}\right), \tag{6}$$

whereas the pressure in CD is represented by (5).

For convenience we will take as our origin in the remaining part of this paper the discontinuity BC. Then we have

$$p_B = p_{AB_{x=0}} = F(t) + f(t), \tag{7}$$

whereas

$$p_C = p_{CD_{x=0}} = g(t). \tag{8}$$

Introducing (7) and (8) into (1) leads to our first relation between the incident, reflected, and transmitted waves at $x = 0$:

$$F(t) + f(t) = g(t). \tag{9}$$

We will now consider the velocity which is connected with the pressure wave (3). This relation could be obtained directly by integration of the Euler equation, using (3), but we will do it in a more elementary way. To a small element of fluid in a tube with radius r and length (Δx) we will apply Newton's law

$$K = m a, \tag{10}$$

in which K represents a force which gives to a mass m an acceleration a. The volume of that element is $\pi r^2 \Delta x$. The mass m is therefore $\rho \pi r^2 \Delta x$, ρ being the density.

If the velocity is represented by $v(t)$, the acceleration a is, on the average,

$$a = \frac{v(t+\Delta t) - v(t)}{\Delta t}.$$

The force K on the element is the difference between the force due to the pressure on the left-hand side,

$$p(x)\,\pi r^2,$$

and that on the right-hand side,

$$p(x+\Delta x)\,\pi r^2.$$

Therefore

$$K = \{p(x) - p(x+\Delta x)\}\,\pi r^2.$$

Introducing these expressions for the mass, acceleration, and force into (10), we obtain

$$\{p(x) - p(x+\Delta x)\}\,\pi r^2 = \rho \pi r^2 \Delta x \frac{v(t+\Delta t) - v(t)}{\Delta t},$$

or, simplifying,

$$\frac{p(x) - p(x+\Delta x)}{\Delta x} = \rho \frac{v(t+\Delta t) - v(t)}{\Delta t}, \tag{11}$$

which is an approximate form of the Euler equation mentioned above.

If p is given by (3) we have, introducing (3) into (11) and rearranging,

$$v(t+\Delta t) - v(t) = \frac{1}{\rho} \frac{F\left(t-\frac{x}{c}\right) - F\left(t-\frac{x+\Delta x}{c}\right)}{\frac{\Delta x}{\Delta t}}. \tag{12}$$

The denominator $\Delta x/\Delta t$ is the velocity c,

$$\frac{\Delta x}{\Delta t} = c, \tag{13}$$

from which we find

$$\frac{\Delta x}{c} = \Delta t. \tag{14}$$

Introducing (13) and (14) into (12) we obtain after some new arrangements:

$$v(t+\Delta t) - v(t) = \frac{1}{\rho c}\left\{F\left(t-\frac{x}{c}\right) - F\left(t-\Delta t-\frac{x}{c}\right)\right\},$$

or

$$v(t+\Delta t) - v(t) = \frac{1}{\rho c} F\left[\left\{(t-\Delta t) - \frac{x}{c}\right\} + \Delta t\right] - \left[-\frac{1}{\rho c} F\left\{(t-\Delta t) - \frac{x}{c}\right\}\right]. \tag{15}$$

From (15) we see, particularly if we write t instead of $(t - \Delta t)$ in the second member, that

$$v(t) = \frac{1}{\rho c} F\left(t-\frac{x}{c}\right), \tag{16}$$

which is the relation we have been looking for. Correspondingly, the velocity associated with (4) is given by

$$v(t) = -\frac{1}{\rho c} f\left(t+\frac{x}{c}\right) \tag{17}$$

and that associated with (5) by

$$v(t) = \frac{1}{\rho c'} g\left(t-\frac{x}{c'}\right). \tag{18}$$

The total velocity in AB associated with the pressure given in (6) is then

$$v_{AB} = \frac{1}{\rho c} F\left(t-\frac{x}{c}\right) - \frac{1}{\rho c} f\left(t+\frac{x}{c}\right), \tag{19}$$

whereas the velocity in CD is given by (18). Equations (6) and (19) are the basic equations of the theory of the water-hammer phenomenon (Allievi, 1903).

Then we have

$$v_B = v_{AB_{x=0}} = \frac{1}{\rho c} F(t) - \frac{1}{\rho c} f(t) \tag{20}$$

and

$$v_C = v_{CD_{x=0}} = \frac{1}{\rho c'} g(t). \tag{21}$$

Introducing (20) and (21) into (2), we obtain:

$$\pi R^2 \left\{ \frac{1}{\rho c} F(t) - \frac{1}{\rho c} f(t) \right\} = \pi r^2 \left\{ \frac{1}{\rho c'} g(t) \right\}$$

or, simplifying,

$$F(t) - f(t) = \frac{r^2}{R^2} \frac{c}{c'} g(t). \tag{22}$$

The equations (9) and (22) give us two linear equations for the two unknown ratios $f(t)/F(t)$ and $g(t)/F(t)$.

Solving (9) and (22) for these unknowns, we find

$$\frac{f(t)}{F(t)} = \frac{1 - \frac{r^2}{R^2} \frac{c}{c'}}{1 + \frac{r^2}{R^2} \frac{c}{c'}}$$

or, after simplification,

$$\frac{f(t)}{F(t)} = \frac{R^2 c' - r^2 c}{R^2 c' + r^2 c}. \tag{23}$$

Similarly,

$$\frac{g(t)}{F(t)} = \frac{2R^2 c'}{R^2 c' + r^2 c}. \tag{24}$$

It may look paradoxical that the left-hand sides of (23) and (24) seem to depend on t, whereas the right-hand sides are independent of t; the velocities depend in general on the geometrical and elastic properties of the tube, as we will see, but not on t. However, in the case where

$$F\left(t - \frac{x}{c}\right) = A \sin \omega \left(t - \frac{x}{c}\right), \tag{25}$$

$$f\left(t + \frac{x}{c}\right) = B \sin \left\{ \omega \left(t + \frac{x}{c}\right) + \phi \right\}, \tag{26}$$

$$g\left(t - \frac{x}{c}\right) = D \sin \left\{ \omega \left(t - \frac{x}{c}\right) + \psi \right\}, \tag{27}$$

in which ϕ and ψ represent the phase differences of the incident, reflected, and transmitted waves, we have, by introducing (25), (26), and (27) into

(9) and (22), after substituting $x = 0$ in the last two equations, and denoting, for abbreviation, $(r^2/R^2)\,(c/c') = k$:

$$A \sin \omega t + B \sin (\omega t + \phi) = D \sin (\omega t + \psi) \tag{28}$$

and

$$A \sin \omega t - B \sin (\omega t + \phi) = k D \sin (\omega t + \psi)\,. \tag{29}$$

Because (1), (2), (9), and (22), and therefore (28) and (29), hold for all values of t, the coefficients of $\sin \omega t$ and those of $\cos \omega t$ in both sides of each equation must be equal, which leads to:

$$A + B \cos \phi = D \cos \psi\,, \tag{30}$$

$$B \sin \phi = D \sin \psi\,, \tag{31}$$

$$A - B \cos \phi = k D \cos \psi\,, \tag{32}$$

$$-B \sin \phi = k D \sin \psi\,. \tag{33}$$

These four equations must be solved to find the four unknowns B/A, D/A, ϕ, and ψ. Because k is in general not equal to -1, (31) and (33) can only be simultaneously satisfied if

$$\sin \phi = 0 \tag{34}$$

and

$$\sin \psi = 0\,. \tag{35}$$

Equation (34) is satisfied if

$$\phi = m\pi\,, \qquad m = 0, \pm 1, \ldots \tag{36}$$

and (35) if

$$\psi = n\pi\,, \qquad n = 0, \pm 1, \ldots, \tag{37}$$

corresponding to a reflection and transmission in or out of phase. But for these values of ϕ and ψ the ratios

$$\frac{f(t)}{F(t)} = \frac{B \sin (\omega t + \phi)}{A \sin \omega t}$$

and

$$\frac{g(t)}{F(t)} = \frac{D \sin (\omega t + \psi)}{A \sin \omega t}$$

are independent of t and, except for the sign, equal to B/A and D/A, the ratio of the amplitudes. This is the reason that we will call those ratios the reflection and the transmission coefficient, respectively. The reflection coefficient is then given by (23) in terms of the radii and the velocities, the transmission coefficient similarly by (24). To get those coefficients in terms of only the geometrical and elastic properties we have to express the velocities in terms of those quantities. Here we could use the results of the more refined treatment, given in the Appendix, which takes into account the viscous properties of the fluid and the elastic properties of the wall,

both in some detail. We will also give here an elementary treatment which, though crude, exhibits all the features essential for our present purposes. However, before doing that we would like to point out an extension of formulas (23) and (24) for the case in which there is a branching of a vessel (Fig. 2).

The result for the reflection coefficient, in which we are here mostly interested, is:

$$\frac{f(t)}{F(t)} = \frac{1 - \frac{r_1^2}{R^2}\frac{c}{c_1} - \frac{r_2^2}{R^2}\frac{c}{c_2}}{1 + \frac{r_1^2}{R^2}\frac{c}{c_1} + \frac{r_2^2}{R^2}\frac{c}{c_2}}. \tag{38}$$

The generalization of this formula to the case of any number of branchings is obvious.

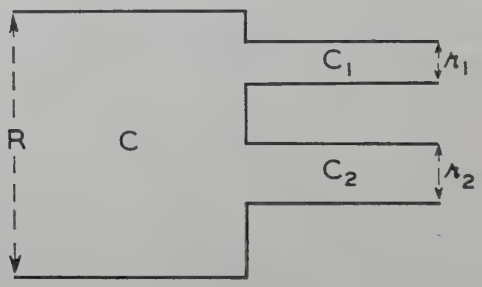

FIGURE 2

To derive the relation between the velocity c of wave propagation and the geometrical and elastic properties of the system we proceed as follows. First we derive the relation between the pressure p in an elastic tube and the tension σ in the wall (Fig. 3). The force on a piece of the tube with a length L (Fig. 3) due to the pressure on the inner wall of that piece is, according to a well-known theorem of physics,

$$p \times \text{area } ABCD = p \times 2rL . \tag{39}$$

The force on that same piece due to the tension in the wall is (Fig. 3):

$$\sigma \times \text{area } (ADIH + BCGF) = \sigma \times (\delta L + \delta L) = 2\sigma\,\delta L . \tag{40}$$

In equilibrium the last two forces are equal, therefore

$$2rLp = 2\,\delta L\sigma$$

or

$$\sigma = \frac{r}{\delta}p . \tag{41}$$

From (41) we see that if the pressure is changed from the value $p(t)$ to a value $p(t+\Delta t)$ the tension σ is changed from $\sigma(t)$, given by (41), if we take $p = p(t)$ to a value $\sigma(t+\Delta t)$, which is correspondingly given by*

$$\sigma\,(t+\Delta t) = \frac{r}{\delta}\,p\,(t+\Delta t)\,.$$

The change in tension is, therefore,

$$\sigma\,(t+\Delta t) - \sigma\,(t) = \frac{r}{\delta}\{\,p\,(t+\Delta t) - p\,(t)\,\}. \tag{42}$$

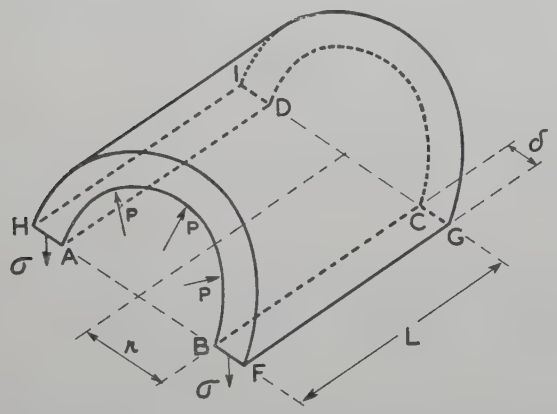

FIGURE 3

Assuming Hooke's law to hold, we have

$$r\,(t+\Delta t) - r\,(t) = \{\,\sigma\,(t+\Delta t) - \sigma\,(t)\,\}\frac{r\,(t)}{E}, \tag{43}$$

in which E is the elasticity modulus.

Introducing (42) into (43), we obtain

$$r\,(t+\Delta t) - r\,(t) = \{\,p\,(t+\Delta t) - p\,(t)\,\}\frac{r^2}{\delta E}. \tag{44}$$

The corresponding increase in volume of an element with length Δx is given by, using (44),

$$2\pi r\{\,r\,(t+\Delta t) - r\,(t)\,\}\Delta x = \frac{2\pi r^3}{\delta E}\,\Delta x\{\,p\,(t+\Delta t) - p\,(t)\,\}. \tag{45}$$

* Here we neglect changes in r and δ as is usually done in the water-hammer theory (cf. Jaeger, 1949, p. 253). It can be shown that this approximation is justified if

$$\frac{r\,(t)}{E\delta\,(t)}\,p\,(t+\Delta t) \qquad \text{and} \qquad \frac{r\,(t)}{E\delta\,(t+\Delta t)}\,p\,(t+\Delta t)$$

are small compared with 1.

The time rate of increase of the volume is therefore

$$\frac{2\pi r^3}{\delta E}\,\Delta x\,\frac{p\,(t+\Delta t)\,-\,p\,(t)}{\Delta t}\,. \tag{46}$$

Assuming the fluid to be incompressible, this time rate of increase of the volume is equal to the difference between the flow into the element from the left-hand side per unit of time,

$$\pi r^2\,v\,(x)\,,$$

and the flow out of the element to the right-hand side per unit of time

$$\pi r^2\,v\,(x+\Delta x)\,.$$

Therefore we have

$$\frac{2\pi r^3}{\delta E}\,\Delta x\,\frac{p\,(t+\Delta t)\,-\,p\,(t)}{\Delta t} = \pi r^2\,v\,(x)\,-\pi r^2\,v\,(x+\Delta x)$$

or, simplifying and rearranging,

$$\frac{v\,(x)\,-\,v\,(x+\Delta x)}{\Delta x} = \frac{2r}{\delta E}\,\frac{p\,(t+\Delta t)\,-\,p\,(t)}{\Delta t}\,. \tag{47}$$

It should be realized that both the velocity v and the pressure p are functions of the two variables x and t. Therefore we will write (47) more completely in the form

$$\frac{v\,(x,\,t)\,-\,v\,(x+\Delta x,\,t)}{\Delta x} = \frac{2r}{\delta E}\,\frac{p\,(x,\,t+\Delta t)\,-\,p\,(x,\,t)}{\Delta t}\,. \tag{48}$$

Similarly (11) should be written more completely as

$$\frac{p\,(x,\,t)\,-\,p\,(x+\Delta x,\,t)}{\Delta x} = \rho\,\frac{v\,(x,\,t+\Delta t)\,-\,v\,(x,\,t)}{\Delta t}\,. \tag{49}$$

Now writing (48) for $t+\Delta t$ instead of for t, we obtain

$$\frac{v\,(x,\,t+\Delta t)\,-\,v\,(x+\Delta x,\,t+\Delta t)}{\Delta x} = \frac{2r}{\delta E}\,\frac{p\,(x,\,t+2\Delta t)\,-\,p\,(x,\,t+\Delta t)}{\Delta t}\,. \tag{50}$$

Subtracting equation (48) from (50) we have, after rearrangement,

$$\begin{aligned}&[\{\,v\,(x,\,t+\Delta t)-v\,(x,\,t)\,\}-\{\,v\,(x+\Delta x,\,t+\Delta t)-v\,(x+\Delta x,\,t)\,\}]\,/\Delta x\\ &=\left(\frac{2r}{\delta E}\right)[\{\,p\,(x,\,t+2\Delta t)-p\,(x,\,t+\Delta t)\,\}-\{\,p\,(x,\,t+\Delta t)\,-\,p\,(x,\,t)\,\}]\,/\Delta t\,.\end{aligned} \tag{51}$$

Multiplying both members of (51) by $\rho/\Delta t$ we find

$$\rho\,[\{\,v\,(x,\,t+\Delta t)\,-\,v\,(x,\,t)\,\}/\Delta t-\{\,v\,(x+\Delta x,\,t+\Delta t)$$

$$-\,v\,(x+\Delta x,\,t)\,\}/\Delta t]\,/\,\Delta x=\left(\frac{2\,r\,\rho}{\delta E}\right)[\{\,p\,(x,\,t+2\Delta t) \quad (52)$$

$$-\,p\,(x,\,t+\Delta t)\,\}-\{\,p\,(x,\,t+\Delta t)\,-\,p\,(x,\,t)\,\}]\,/\,(\Delta t)^2\,.$$

For the two terms in the numerator of the left-hand side of (52) we use (49) and an equation similar to (49), only with $(x + \Delta x)$ instead of x. We then obtain

$$[\{\,p\,(x,\,t)\,-\,p\,(x+\Delta x,\,t)\,\}/\Delta x-\{\,p\,(x+\Delta x,\,t)$$

$$-\,p\,(x+2\Delta x,\,t)\,\}/\Delta x]\,/\,\Delta x=\left(\frac{2\,r\,\theta}{\delta E}\right)[\{\,p\,(x,\,t+2\Delta t) \quad (53)$$

$$-\,p\,(x,\,t+\Delta t)\,\}-\{\,p\,(x,\,t+\Delta t)\,-\,p\,(x,\,t)\,\}]\,/\,(\Delta t)^2\,.$$

Or, simplifying,

$$\frac{p\,(x,\,t)\,-2p\,(x+\Delta x,\,t)\,+p\,(x+2\Delta x,\,t)}{(\Delta x)^2}$$

$$=\frac{2\,r\,\rho}{\delta E}\,\frac{p\,(x,\,t+2\Delta t)\,-2p\,(x,\,t+\Delta t)\,+p\,(x,\,t)}{(\Delta t)^2}. \quad (54)$$

We see that (54) is satisfied if

$$p\,(x+\Delta x,\,t)\,=p\,(x,\,t+\Delta t)\,, \quad (55)$$

$$p\,(x+2\Delta x,\,t)\,=p\,(x,\,t+2\Delta t)\,, \quad (56)$$

and

$$\frac{\Delta x}{\Delta t}=\pm\sqrt{\frac{\delta E}{2\,r\,\rho}}. \quad (57)$$

Equations (55) and (56) describe a wave which is propagated without deformation. According to (55) the value of the pressure at the point with abscissa $x + \Delta x$ at the time t is exactly the same as that at the point with abscissa x at the time $t + \Delta t$, and (56) has a similar meaning. The velocity c of propagation of the wave is given by (57) in terms of the thickness δ of the wall, the elasticity modulus E of the wall, the radius r of the tube, and the density ρ of the fluid

$$c=\sqrt{\frac{\delta E}{2\,r\,\rho}}. \quad (58)$$

In the case of a plus sign in (57) the wave is propagated in the direction of the negative x-axis, as will be obvious from the explanation above of why (55) and (56) describe a propagating wave. In the case of a minus sign in

(57) the direction of propagation of the wave is in the direction of the positive x-axis. Formula (58) is a special case of the formula used for the propagation of pressure waves in the theory of the water-hammer phenomenon (Jaeger, *loc. cit.*), namely, for an imcompressible fluid. The most general form of this formula appears to have been derived for the first time by D. J. Korteweg (1878). Treatments taking into account the viscosity of the fluid (Witzig, 1914, or the Appendix to this paper) lead to an approximate formula in which the dependence of c on δ, E, r, and ρ is the same and only the numerical coefficient in front of the square root is different.

From (58) we find

$$c = \sqrt{\frac{\delta E}{2R\rho}}$$

for the velocity c in AB and

$$c' = \sqrt{\frac{\delta_1 E_1}{2r\rho}}$$

for the velocity c' in CD and we introduce these results into (23). We then obtain for the reflection coefficient $\eta = f(t)/F(t)$ the formula

$$\eta = \frac{R^2\sqrt{\frac{\delta_1 E_1}{2r\rho}} - r^2\sqrt{\frac{\delta E}{2R\rho}}}{R^2\sqrt{\frac{\delta_1 E_1}{2r\rho}} + r^2\sqrt{\frac{\delta E}{2R\rho}}}$$

or, after simplification,

$$\eta = \frac{\sqrt{\frac{\delta_1}{\delta}\frac{E_1}{E}} - \left(\frac{r}{R}\right)^{5/2}}{\sqrt{\frac{\delta_1}{\delta}\frac{E_1}{E}} + \left(\frac{r}{R}\right)^{5/2}}. \tag{59}$$

Equation (59) gives η in terms of the ratios r/R, which might be called the "coarctation ratio," δ_1/δ, and E_1/E. In the case of a coarctation in which there is only a change in diameter of the vessel $\delta_1 = \delta$, $E_1 = E$, and, therefore,

$$\eta = \frac{1 - \left(\frac{r}{R}\right)^{5/2}}{1 + \left(\frac{r}{R}\right)^{5/2}}. \tag{60}$$

The graph of η as a function of r/R is shown in Figure 4.

For $r = R$, $\eta = 1$, as it should, and for $r = R$, $\eta = 0$, which should also be the case.

But if $\delta_1 \neq \delta$, and/or $E_1 \neq E$, or for any case in which $\delta_1 E_1 \neq \delta E$, the reflection coefficient η is given by formula (59). In this case, even if $r = R$, $\eta \neq 0$, and the pressure waves will be reflected.

For this case the reflection coefficient is

$$\eta = \frac{\sqrt{\frac{\delta_1}{\delta}\frac{E_1}{E}} - 1}{\sqrt{\frac{\delta_1}{\delta}\frac{E_1}{E}} + 1}. \tag{61}$$

This would be the case if there is a local thickening of the wall, so that $\delta_1 \neq \delta$, as in arteriosclerosis, or other pathological conditions in which $E_1 \neq E$ resulting from a locally changed structure of the wall material.

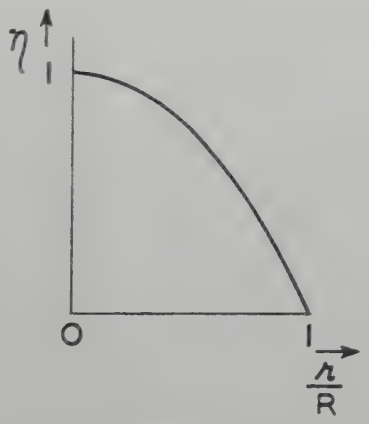

FIGURE 4

In all these cases the reflection coefficient might therefore give important clues for clinical applications.

Let us now investigate how the pressure pattern might inform us about the reflection coefficient. Therefore we will take here as an illustration the simple case in which the incident wave is purely sinusoidal, in other words the functions

$$F\left(t-\frac{x}{c}\right) \quad \text{and} \quad f\left(t+\frac{x}{c}\right)$$

are given by (25) and (26). In the latter we take $\phi = 0$ which corresponds to $m = 0$ in (36). Then, as shown above in connection with (36) and (37),

$$\eta = \frac{f(t)}{F(t)} = \frac{B}{A}$$

and therefore $B = \eta A$.

The pressure at any point with abscissa x at any time t is then given by [similar to (6)]

$$p = A \sin \omega \left(t - \frac{x}{c}\right) + \eta A \sin \omega \left(t + \frac{x}{c}\right). \tag{62}$$

We may write the last equation

$$p = A\,(1+\eta) \cos \omega \frac{x}{c} \sin \omega t - A\,(1-\eta) \sin \omega \frac{x}{c} \cos \omega t\,. \tag{63}$$

From (63) we see that, whereas for $\eta = 1$ (complete reflection)

$$p = 2A \cos \omega \frac{x}{c} \sin \omega t\,, \tag{64}$$

which represents a standing wave with nodes for

$$\omega \frac{x}{c} = \frac{\pi}{2} + l\pi \qquad l = 0\,, \pm 1, \pm 2 \ldots, \tag{65}$$

the superposition of a propagated wave and a partially reflected wave never produces any standing waves. In fact, the pressure represented by (63) has no nodes at all. This makes us wonder if in practical cases, where there is never complete reflection, standing waves are ever observed and makes us critical about claims of observed existence of standing wave patterns, particularly in complicated physiological cases. What can really be observed, at most, are minima and maxima of the amplitude of the wave produced by the superposition of the two waves advancing in opposite directions, which occur at the so-called "pseudo" nodes and antinodes (cf. Wood, 1930, p. 281). However, in the simple case treated above, the latter are always a finite distance apart; in fact, a quarter of a wave length. However no matter what the case may be, the pattern caused by the superposition of an advancing wave and the wave resulting from it by incomplete reflection gives clues as to the reflection coefficient. As a matter of fact, in the simple case treated above the maximum and minimum amplitudes are $A(1 + \eta)$ and $A(1 - \eta)$. By knowing A, which is determined by the stroke volume, η can be determined. From formulae (59), (60), or (61) we might then obtain information about δ_1/δ, E_1/E, or r/R, depending on the circumstances. In this way clinically important new clues, which are of a quantitative nature, might be obtained from a study of the pressure pattern, if we study the reflection condition of pressure waves in the aorta or other blood vessels. Crude as this theory is (obviously there is more than enough room left for improvement) we are led to believe that Apéria (*loc. cit.*) and Porjé (*loc. cit.*) were right in stressing the development of a quantitative study of the reflection conditions with which they themselves started.

APPENDIX

To derive the dependence of the velocity of propagation of pressure waves in a fluid enclosed within an elastic tube we will follow and extend the treatment given by Witzig (*loc. cit.*), which is probably the most advanced one ever published but which does not seem to have attracted much attention.

The Navier-Stokes equations for the axial-symmetric flow of a viscous fluid in a cylindrical tube are (Lamb, 1932)

$$\rho\left(\frac{\partial v_z}{\partial t}+v_z\frac{\partial v_z}{\partial z}+v_r\frac{\partial v_z}{\partial r}\right)=\mu\left(\frac{\partial^2 v_z}{\partial z^2}+\frac{1}{r}\frac{\partial v_z}{\partial r}+\frac{\partial^2 v_z}{\partial r^2}\right)-\frac{\partial p}{\partial z}, \quad (66)$$

$$\rho\left(\frac{\partial v_r}{\partial t}+v_z\frac{\partial v_r}{\partial z}+v_r\frac{\partial v_r}{\partial r}\right)=\mu\left(\frac{\partial^2 v_r}{\partial z^2}+\frac{1}{r}\frac{\partial v_r}{\partial r}+\frac{\partial^2 v_r}{\partial r^2}\right)-\frac{\partial p}{\partial r}. \quad (67)$$

Assuming that the gradients of the velocities are so small that the non-linear terms may be neglected, we have

$$\frac{\partial v_z}{\partial t}=\gamma\left(\frac{\partial^2 v_z}{\partial z^2}+\frac{1}{r}\frac{\partial v_z}{\partial r}+\frac{\partial^2 v_z}{\partial r^2}\right)-\frac{1}{\rho}\frac{\partial p}{\partial z}, \quad (68)$$

$$\frac{\partial v_r}{\partial t}=\gamma\left(\frac{\partial^2 v_r}{\partial z^2}+\frac{1}{r}\frac{\partial v_r}{\partial r}+\frac{\partial^2 v_r}{\partial r^2}\right)-\frac{1}{\rho}\frac{\partial p}{\partial r}, \quad (69)$$

in which $\gamma = \mu/\rho$.

Assuming furthermore that the fluid is incompressible, the continuity equation is:

$$\frac{\partial v_z}{\partial z}+\frac{1}{r}\frac{\partial}{\partial r}\left(r\frac{\partial v_r}{\partial r}\right)=0. \quad (70)$$

This equation is satisfied if

$$v_z=-\frac{1}{r}\frac{\partial \psi}{\partial r}, \quad (71)$$

$$v_r=\frac{1}{r}\frac{\partial \psi}{\partial z}, \quad (72)$$

ψ being Stokes' stream function.

Elimination of p from (68) and (69) by their differentiation to r and z, respectively, and afterward subtraction of the results leads to

$$\left\{\frac{\partial}{\partial t}-\gamma\left(\frac{\partial^2}{\partial z^2}+\frac{1}{r}\frac{\partial}{\partial r}+\frac{\partial^2}{\partial r^2}-\frac{1}{r^2}\right)\right\}\left(\frac{\partial v_r}{\partial z}-\frac{\partial v_z}{\partial r}\right)=0. \quad (73)$$

From (71) and (72) we derive

$$\frac{\partial v_r}{\partial z}-\frac{\partial v_z}{\partial r}=\frac{1}{r}\left(\frac{\partial^2 \psi}{\partial z^2}-\frac{1}{r}\frac{\partial \psi}{\partial r}+\frac{\partial^2 \psi}{\partial r^2}\right). \quad (74)$$

Introducing (74) into (73) we obtain

$$\left\{\frac{\partial}{\partial t}-\gamma\left(\frac{\partial^2}{\partial z^2}+\frac{1}{r}\frac{\partial}{\partial r}+\frac{\partial^2}{\partial r^2}-\frac{1}{r^2}\right)\right\}\left\{\frac{1}{r}\left(\frac{\partial^2\psi}{\partial z^2}-\frac{1}{r}\frac{\partial\psi}{\partial r}+\frac{\partial^2\psi}{\partial r^2}\right)\right\}=0 \quad (75)$$

or

$$\left\{\frac{\partial}{\partial t}-\gamma\left(\frac{\partial^2}{\partial z^2}+\frac{1}{r}\frac{\partial}{\partial r}+\frac{\partial^2}{\partial r^2}-\frac{1}{r^2}\right)\right\}\left(\frac{\partial^2}{\partial z^2}+\frac{1}{r}\frac{\partial}{\partial r}+\frac{\partial^2}{\partial r^2}-\frac{1}{r^2}\right)\left(\frac{\psi}{r}\right)=0\,. \quad (76)$$

For abbreviation, let us denote symbolically

$$\frac{\partial^2}{\partial z^2}+\frac{1}{r}\frac{\partial}{\partial r}+\frac{\partial^2}{\partial r^2}-\frac{1}{r^2}=D\,. \quad (77)$$

Instead of (76) we then have

$$\left(\frac{\partial}{\partial t}-\gamma D\right)D\left(\frac{\psi}{r}\right)=0\,. \quad (78)$$

Following Witzig (*loc. cit.*), who quotes G. G. Stokes (1819) for this approach, we will suppose that it is possible to put

$$\psi=\psi_1+\psi_2\,, \quad (79)$$

in which ψ_1 is such that

$$D\left(\frac{\psi_1}{r}\right)=0\,; \quad (80)$$

whereas ψ_2 satisfies

$$\left(\frac{\partial}{\partial t}-\gamma D\right)\frac{\psi_2}{r}=0\,. \quad (81)$$

Substitution of (77) into (80) and (81) leads to

$$\frac{\partial^2\psi_1}{\partial z^2}-\frac{1}{r}\frac{\partial\psi_1}{\partial r}+\frac{\partial^2\psi_1}{\partial r^2}=0 \quad (82)$$

and

$$\frac{\partial^2\psi_2}{\partial z^2}-\frac{1}{r}\frac{\partial\psi_2}{\partial r}+\frac{\partial^2\psi_2}{\partial r^2}-\frac{1}{\gamma}\frac{\partial\psi_2}{\partial t}=0\,. \quad (83)$$

These equations allow particular solutions of the form

$$\psi_1=F(r)\;e^{i\omega[t-(z/c)]} \quad (84)$$

and

$$\psi_2=G(r)\;e^{i\omega[t-(z/c)]}\,. \quad (85)$$

Substitution of ψ_1 from (84) into (82) leads to the next equation for $F(r)$:

$$\frac{d^2F}{dr^2}-\frac{1}{r}\frac{dF}{dr}-\frac{\omega^2}{c^2}F=0\,. \quad (86)$$

The solution of this equation is given by

$$F(r) = r\left\{aJ_1\left(i\frac{\omega}{c}r\right) + bY_1\left(i\frac{\omega}{c}r\right)\right\}, \tag{87}$$

in which

$$J_1\left(i\frac{\omega}{c}r\right) \quad \text{and} \quad Y_1\left(i\frac{\omega}{c}r\right)$$

are Bessel functions of the first order, and a and b are arbitrary constants.

Because $F(0)$ is finite, whereas

$$\lim_{r\to 0} Y_1\left(i\frac{\omega}{c}r\right) = \infty, \tag{88}$$

we must have

$$b = 0. \tag{89}$$

Therefore, introducing (89) into (87) we obtain

$$F(r) = arJ_1\left(i\frac{\omega}{c}r\right). \tag{90}$$

Because

$$iJ_1\left(i\frac{\omega}{c}r\right)$$

is real, we will write $a = iA$ and (90) becomes

$$F(r) = AirJ_1\left(i\frac{\omega}{c}r\right). \tag{91}$$

Introducing (91) into (84) gives us

$$\psi_1 = AirJ_1\left(i\frac{\omega}{c}r\right)e^{i\omega[t-(z/c)]}. \tag{92}$$

Substitution of (85) into (83) yields

$$\frac{d^2G}{dr^2} - \frac{1}{r}\frac{dG}{dr} - \frac{\omega^2}{c^2}G - \frac{i\omega}{\gamma}G = 0. \tag{93}$$

If we put

$$\frac{\omega^2}{c^2} + \frac{i\omega}{\gamma} = \alpha^2 \tag{94}$$

we obtain from (93)

$$\frac{d^2G}{dr^2} - \frac{1}{r}\frac{dG}{dr} - \alpha^2 G = 0, \tag{95}$$

which equation is similar to (86). Therefore we have

$$\psi_2 = BirJ_1(ia\,r)\,e^{i\omega[t-(z/c)]}. \tag{96}$$

From (79), (92), and (96) we obtain

$$\psi = r\left\{AirJ_1\left(i\frac{\omega}{c}r\right) + BirJ_1(ia\,r)\,e^{i\omega[t-(z/c)]}\right\}. \tag{97}$$

To derive a relation between the stream function ψ and the pressure p, we obtain from (68), (69), (71), and (72)

$$-\frac{1}{r}\frac{\partial^2\psi}{\partial r\,\partial t}-\frac{\gamma}{r}\frac{\partial}{\partial r}\left(-\frac{\partial^2\psi}{\partial z^2}+\frac{1}{r}\frac{\partial\psi}{\partial r}-\frac{\partial^2\psi}{\partial r^2}\right)=-\frac{1}{\rho}\frac{\partial p}{\partial z}, \tag{98}$$

$$\frac{1}{r}\frac{\partial^2\psi}{\partial z\,\partial t}-\frac{\gamma}{r}\frac{\partial}{\partial z}\left(\frac{\partial^2\psi}{\partial z^2}-\frac{1}{r}\frac{\partial\psi}{\partial r}+\frac{\partial^2\psi}{\partial r^2}\right)=-\frac{1}{\rho}\frac{\partial p}{\partial r}. \tag{99}$$

Addition of equations (82) and (83) yields

$$\frac{\partial^2\psi}{\partial z^2}-\frac{1}{r}\frac{\partial\psi}{\partial r}+\frac{\partial^2\psi}{\partial r^2}=\frac{1}{\gamma}\frac{\partial\psi_2}{\partial t}. \tag{100}$$

Substitution of (100) into (98) and (99) leads to

$$-\frac{1}{r}\frac{\partial^2\psi}{\partial r\partial t}-\frac{\gamma}{r}\frac{\partial}{\partial r}\left(-\frac{1}{\gamma}\frac{\partial\psi_2}{\partial t}\right)=-\frac{1}{\rho}\frac{\partial p}{\partial z}, \tag{101}$$

$$\frac{1}{r}\frac{\partial^2\psi}{\partial z\partial t}-\frac{\gamma}{r}\frac{\partial}{\partial z}\left(\frac{1}{\gamma}\frac{\partial\psi_2}{\partial t}\right)=-\frac{1}{\rho}\frac{\partial p}{\partial r}. \tag{102}$$

Because of (79) we have

$$\frac{\partial p}{\partial z}=\frac{\rho}{r}\frac{\partial^2\psi_1}{\partial r\partial t} \tag{103}$$

and

$$\frac{\partial p}{\partial z}=-\frac{\rho}{r}\frac{\partial^2\psi_1}{\partial z\,\partial t}. \tag{104}$$

Multiplication of (103) and (104) by r and then differentiation of the resulting equations to z and r, respectively, and addition of the results yields

$$\frac{\partial^2 p}{\partial z^2}+\frac{1}{r}\frac{\partial p}{\partial r}+\frac{\partial^2 p}{\partial r^2}=0. \tag{105}$$

This equation allows a particular solution of the form

$$p=H(r)\,e^{i\omega[t-(z/c)]}. \tag{106}$$

Substitution of (106) into (105) leads to

$$\frac{d^2H}{dr^2}+\frac{1}{r}\frac{dH}{dr}-\frac{\omega^2}{c^2}H=0. \tag{107}$$

The solution of this equation is:

$$H=DJ_0\left(i\frac{\omega}{c}r\right)+EY_0\left(i\frac{\omega}{c}r\right), \tag{108}$$

in which

$$J_0\left(i\frac{\omega}{c}r\right) \quad \text{and} \quad Y_0\left(i\frac{\omega}{c}r\right)$$

are the Bessel functions of the order zero.

Because

$$\lim_{r\to 0} Y_0\left(i\frac{\omega}{c}r\right) = \infty\,, \tag{109}$$

whereas $p(0)$ and therefore $H(0)$ are finite we must have

$$E = 0\,. \tag{110}$$

Substitution of (110) into (108) and the result into (106) yields

$$p = DJ_0\left(i\frac{\omega}{c}r\right)e^{i\omega[t-(z/c)]}\,. \tag{111}$$

From (92), (103), and (111) we have

$$D = -A\rho\omega\,. \tag{112}$$

Introducing (112) into (111) we obtain

$$p = -A\rho\omega J_0\left(i\frac{\omega}{c}r\right)e^{i\omega[t-(z/c)]}\,. \tag{113}$$

Equations (71) and (72), together with (97), yield

$$v_z = \left\{A\frac{\omega}{c}J_0\left(i\frac{\omega}{c}r\right)+BaJ_0(iar)\right\}e^{i\omega[t-(z/c)]} \tag{114}$$

and

$$v_r = \left\{-A\frac{\omega}{c}J_1\left(i\frac{\omega}{c}r\right)-BaJ_1(iar)\right\}e^{i\omega[t-(z/c)]}\,. \tag{115}$$

Assuming that the wave length is sufficiently large so that

$$\left(\frac{\omega}{c}\right)^2 = \left(\frac{2\pi}{\lambda}\right)^2 \ll \left|\frac{i\omega}{\gamma}\right|\,, \tag{116}$$

we have, approximately,

$$a = \sqrt{\frac{i\omega}{\gamma}} = \beta\sqrt{i}\,; \tag{117}$$

whereas

$$J_0\left(i\frac{\omega}{c}r\right) = J_0\left(i2\pi\frac{r}{\lambda}\right) \approx 1$$

and

$$J_1\left(i\frac{\omega}{c}r\right) = J_1\left(i2\pi\frac{r}{\lambda}\right) \approx i\pi\frac{r}{\lambda}\,.$$

Consequently

$$\psi = r\left\{ A\,\frac{\omega r}{2c} + BiJ_1(r\beta\sqrt{-i}) \right\} e^{i\omega[t-(z/c)]}, \tag{118}$$

$$p = -A\rho\omega e^{i\omega[t-(z/c)]}, \tag{119}$$

$$v_z = \left\{ A\,\frac{\omega}{c} + B\beta\sqrt{i}J_0(r\beta\sqrt{-i}) \right\} e^{i\omega[t-(z/c)]}, \tag{120}$$

$$v_r = -\left\{ iA\,\frac{\omega^2 r}{2c^2} + B\,\frac{\omega}{c}J_1(r\beta\sqrt{-i}) \right\} e^{i\omega[t-(z/c)]}. \tag{121}$$

These formulae were given by Witzig (*loc. cit.*).

We will now study the vibrations of the wall and take into account some terms that Witzig neglected. Assuming an infinitely long cylinder and

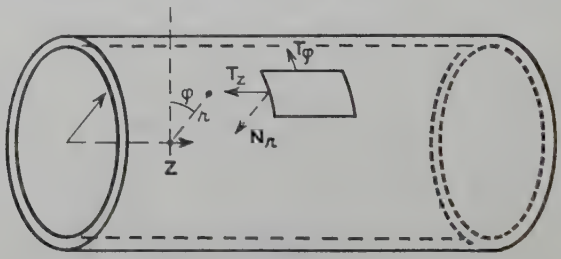

FIGURE 5

axial symmetry, the equations of motion of the wall are (Love, 1944, p. 539, Fig. 5):

$$\frac{\partial T_z}{\partial z} + F_z = 2\rho h\,\frac{\partial^2 u}{\partial t^2}, \tag{122}$$

$$\frac{\partial N_r}{\partial z} - \frac{T\phi}{R} + F_r = 2\rho h\,\frac{\partial^2 w}{\partial t^2}, \tag{123}$$

in which T_z and T_ϕ are the axial and azimuthal tensions, respectively, N_r the radial shearing force in the wall, F_z and F_r the axial and radial components of externally applied forces, ρ the density of the wall material, $2h$ the thickness of the wall, and u and w the axial and radial displacements of the considered element of the wall.

For the axial symmetric case T_z, N_r, and T_ϕ are given by (Love, *loc. cit.*, pp. 544, 530):

$$T_z = D\left\{ \frac{3}{h^2}(\epsilon_1 + \sigma\epsilon_2) + \frac{2 - 2\sigma - 3\sigma^2}{2(1-\sigma)}\,\frac{k_1}{R} \right\}, \tag{124}$$

$$T_\phi = D\left\{ \frac{3}{h^2}(\epsilon_2 + \sigma\epsilon_1) - \frac{\sigma + 2\sigma^2}{2(1-\sigma)}\,\frac{k_1}{R} \right\}, \tag{125}$$

$$N_r = -D\,\frac{\partial k_1}{\partial z}, \tag{126}$$

in which σ is Poisson's ratio for the wall material and the flexurial rigidity D of the wall is given by (Love, *loc. cit.*, p. 503):

$$D = \frac{2Eh^3}{3\,(1-\sigma^2)}, \tag{127}$$

E being Young's modulus.

The expressions for ϵ_1, ϵ_2, and k_1 are given by (Love, *loc. cit.*, p. 543):

$$\epsilon_1 = \frac{\partial u}{\partial z}, \tag{128}$$

$$\epsilon_2 = \frac{w}{r}, \tag{129}$$

$$k_1 = -\frac{\partial^2 w}{\partial z^2}. \tag{130}$$

Introducing (128), (129), and (130) into (124), (125), and (126) and the results into (122) and (123), we obtain

$$2\rho h \frac{\partial^2 u}{\partial t^2} = F_z + \frac{3D}{h^2}\left(\frac{\partial^2 u}{\partial z^2} + \frac{\sigma}{R}\frac{\partial w}{\partial z}\right) - \frac{D}{R}\frac{2-2\sigma-3\sigma^2}{2\,(1-\sigma)}\frac{\partial^3 w}{\partial z^3}, \tag{131}$$

$$2\rho h \frac{\partial^2 w}{\partial t^2} = F_r - \frac{3D}{h^2}\left(\frac{\sigma}{R}\frac{\partial u}{\partial z} + \frac{w}{R^2}\right) - \frac{D}{R^2}\frac{\sigma+2\sigma^2}{2\,(1-\sigma)}\frac{\partial^2 w}{\partial z^2} + D\frac{\partial^4 w}{\partial z^4}. \tag{132}$$

The forces F_z and F_r are the forces exerted by the fluid in the tube on the wall. They are given by (Hopf, 1937, p. 95):

$$F_z = -\mu\left(\frac{\partial v_z}{\partial r} + \frac{\partial v_r}{\partial z}\right)_{r=R}, \tag{133}$$

$$F_r = p - 2\mu\left(\frac{\partial v_r}{\partial r}\right)_{r=R}, \tag{134}$$

after having substituted $r = R$ in the right-hand side, as indicated.

Introducing the expressions (133) and (134) into (131) and (132) we have:

$$2\rho h \frac{\partial^2 u}{\partial t^2} = -\mu\left(\frac{\partial v_z}{\partial r} + \frac{\partial v_r}{\partial z}\right)_{r=R} + \frac{3D}{h^2}\left(\frac{\partial^2 u}{\partial z^2} + \frac{\sigma}{R}\frac{\partial w}{\partial z}\right) - \frac{D}{R}\frac{2-2\sigma-3\sigma^2}{2\,(1-\sigma)}\frac{\partial^3 w}{\partial z^3}, \tag{135}$$

$$2\rho h \frac{\partial^2 w}{\partial t^2} = p - 2\mu\left(\frac{\partial v_r}{\partial r}\right)_{r=R} - \frac{3D}{h^2}\left(\frac{\sigma}{R}\frac{\partial u}{\partial z} + \frac{w}{R^2}\right) - \frac{D}{R}\frac{\sigma+2\sigma^2}{2\,(1-\sigma)}\frac{\partial^2 w}{\partial z^2} + D\frac{\partial^4 w}{\partial z^4}. \tag{136}$$

Assuming no slip of the fluid at the wall, we have also:

$$\frac{\partial u}{\partial t} = (v_z)_{r=R}, \tag{137}$$

$$\frac{\partial w}{\partial t} = (v_r)_{r=R}. \tag{138}$$

Differentiation of equations (135) and (136) to t and introduction of the results (137) and (138) gives us, after neglecting the terms which contain

$$\frac{\partial^3 v_r}{\partial z^3} \quad \text{and} \quad \frac{\partial^4 v_r}{\partial z^4}$$

(which are supposedly sufficiently small), for $r = R$:

$$\frac{\partial^2 v_z}{\partial t^2} = -\gamma\left(\frac{\partial^2 v_z}{\partial t\,\partial r} + \frac{\partial^2 v_r}{\partial t\,\partial r}\right) + \tau\left(\frac{\partial^2 v_z}{\partial z^2} + \frac{\sigma}{R}\frac{\partial v_r}{\partial z}\right), \tag{139}$$

$$\frac{\partial^2 v_r}{\partial t^2} = \varphi\frac{\partial p}{\partial t} - 2\gamma\frac{\partial^2 v_r}{\partial t\,\partial r} - \tau\left(\frac{\sigma}{R}\frac{\partial v_z}{\partial z} + \frac{v_r}{R^2}\right) - \frac{\zeta}{R^2}\frac{\partial^2 v_r}{\partial z^2}, \tag{140}$$

with

$$\gamma = \frac{\mu}{2\rho h}, \tag{141}$$

$$\tau = \frac{3D}{2\rho h^3} = \frac{E}{\rho(1-\sigma^2)}, \tag{142}$$

$$\varphi = \frac{1}{2\rho h}, \tag{143}$$

$$\zeta = \frac{D}{2\rho h}\frac{\sigma + 2\sigma^2}{2(1-\sigma)}. \tag{144}$$

For $\gamma = 0$ and $\zeta = 0$ (139) and (140) reduce to Lamb's equations [cf. Witzig (*loc. cit.*)].

From (119), (120), and (121) we have, for $r = R$,

$$p = -A\rho\omega e^{i\omega[t-(z/c)]},$$

$$v_z = \left\{A\frac{\omega}{c} + B\beta\sqrt{i}J_0(R\beta\sqrt{-i})\right\}e^{i\omega[t-(z/c)]}, \tag{145}$$

$$v_r = -\left\{iA\frac{\omega^2 R}{2c^2} + B\frac{\omega}{c}J_1(R\beta\sqrt{i})\right\}e^{i\omega[t-(z/c)]}. \tag{146}$$

Introducing these equations, together with (145) and (146), into (139) and (140), leads to

$$\alpha A + \gamma B = 0, \tag{147}$$

$$\kappa A + \lambda B = 0, \tag{148}$$

with

$$\alpha = \frac{\omega^3}{c}\left\{1 - \frac{i}{2}\gamma R\frac{\omega}{c^2} - \tau\frac{1}{c^2}\left(1 - \frac{\sigma}{2}\right)\right\}, \tag{149}$$

$$\gamma = i\frac{\omega^2}{R}J_1(R\beta\sqrt{-i})\left\{R\beta\sqrt{-i}\frac{J_0(R\beta\sqrt{-i})}{J_1(R\beta\sqrt{-i})}\left(1 - \frac{\tau}{c^2}\right) - \frac{\gamma R\beta^2}{\omega} - i\frac{\gamma\omega R}{c^2} + \sigma\frac{\tau}{c^2}\right\}, \tag{150}$$

$$\kappa = \frac{i}{2}\frac{\omega^4}{c^2}R + i\phi\rho\omega^2 + \gamma\frac{\omega^3}{c^2} + \frac{i}{2}\frac{\zeta}{R}\frac{\omega^4}{c^4} + i\frac{\tau}{R}\frac{\omega^2}{c^2}\left(\sigma - \tfrac{1}{2}\right), \tag{151}$$

$$\lambda = \frac{\omega}{c}J_1(R\beta\sqrt{-i})\left[-\omega^2 - \frac{2\gamma i\omega}{R}\right\} - 1 + R\beta\sqrt{-i}\frac{J_0(R\beta\sqrt{-i})}{J_1(R\beta\sqrt{-i})}\Big\} - \frac{\zeta}{R^2}\frac{\omega^2}{c^2} - \sigma\frac{\tau}{R^2}R\beta\sqrt{-i}\frac{J_0(R\beta\sqrt{-i})}{J_1(R\beta\sqrt{-i})} + \frac{\tau}{R^2}\Big]. \tag{152}$$

Elimination of A and B from (147) and (148) leads to

$$\alpha\lambda = \gamma\kappa, \tag{153}$$

or, after introducing (149), (150), (151), and (152) into (153) and simplifying,

$$\begin{aligned}\frac{\omega^2}{c^2}\left\{1 - \frac{i}{2}\gamma R\frac{\omega}{c^2} - \frac{\tau}{c^2}\left(1 - \frac{\sigma}{2}\right)\right\}\Big[-\omega^2 - \frac{2i\gamma\omega}{R}\Big\} - 1 + R\beta\sqrt{-i} \\ \times\frac{J_0(R\beta\sqrt{-i})}{J_1(R\beta\sqrt{-i})}\Big\} - \frac{\zeta}{R^2}\frac{\omega^2}{c^2} - \sigma\frac{\tau}{R^2}R\beta\sqrt{-i}\frac{J_0(R\beta\sqrt{-i})}{J_1(R\beta\sqrt{-i})} + \frac{\tau}{R^2}\Big] \\ = i\frac{1}{R}\Big\{R\beta\sqrt{-i}\frac{J_0(R\beta\sqrt{-i})}{J_1(R\beta\sqrt{-i})}\left(1 - \frac{\tau}{c^2}\right) - \frac{\gamma R\beta^2}{\omega} - i\frac{\gamma\omega R}{c^2} \\ + \sigma\frac{\tau}{c^2}\Big\}\Big\{\frac{i}{2}\frac{\omega^4}{c^2}R + i\varphi\rho\omega^2 + \gamma\frac{\omega^3}{c^2} + \frac{i}{2}\frac{\zeta}{R}\frac{\omega^4}{c^4} + i\frac{\tau}{R}\frac{\omega^2}{c^2}\left(\sigma - \tfrac{1}{2}\right)\Big\}.\end{aligned} \tag{154}$$

Neglecting the inertia terms and some other terms which are negligible for plausible values of the parameters: $\gamma \sim 1$, $R \sim 1$, $\omega \sim 10$, $c \sim 10^3$, $\tau \sim 10^6$, $\zeta \sim 10^3$, $\sigma \sim 0.5$, and dropping some terms which Witzig (*loc. cit.*) did not take into account, we find as a check Witzig's formula

$$\{Re\,(c)\}^2 = \frac{Eh}{R\rho}\frac{(P-2)(P-\sigma) + Q^2}{R\rho(P-\sigma)^2 + Q^2}, \tag{155}$$

in which $Re(c)$ is the real part of c, and P and Q are the real and imaginary parts, respectively, of the function

$$R\beta\sqrt{-i}\frac{J_0(R\beta\sqrt{-i})}{J_1(R\beta\sqrt{-i})}$$

which occurs in (154).

Still neglecting the inertia terms, but keeping the terms

$$\frac{\gamma R\beta^2}{\omega} \quad \text{and} \quad \frac{i}{2}\frac{\omega^4}{c^2}R,$$

which are lacking in Witzig's treatment but which may not be negligible, we obtain

$$\{Re(c)\}^2 = \frac{Eh}{R\rho}\frac{(P-2)(P-\frac{1}{2})+Q^2}{(P-\frac{1}{2})^2+Q^2}. \tag{156}$$

For $\sigma = \frac{1}{2}$ we again obtain Witzig's formula. Keeping both inertia terms and the terms mentioned above, we obtain after some lengthy numerical calculations the next result:

$$Re(c) = \sqrt{\frac{Eh}{R\rho}}\left(0.8 + 0.03R\sqrt{\frac{\omega}{\gamma}}\right). \tag{157}$$

As expected, the influence of the viscosity on the velocity of propagation is very slight. The damping is given by the dependence of $Im(c)$ on γ which can be calculated in the same way.

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RESPONSE TIME AND THRESHOLD OF A RANDOM NET

ANATOL RAPOPORT
COMMITTEE ON MATHEMATICAL BIOLOGY
THE UNIVERSITY OF CHICAGO

The response time of a random net is defined as the expected time (measured in the number of synaptic delays) required for the excitation in the net (measured by the fraction of neurons firing per unit time) to reach a certain level. The response time is calculated in terms of the net parameters as a function of the intensity of the outside stimulation. Two principal types of cases are studied, 1) an instantaneous initial stimulation, and 2) continuously applied stimulation. It is shown that for a certain type of net where the required level of excitation is small, the response time-intensity equation reduces to the one derived on the basis of the "one-factor" theory applied to a neural connection. More general assumptions, however, give different types of equations.

The concept of the "net threshold" is defined, and its calculation indicated. The net threshold for instantaneous stimulation is, in general, greater than that for continuous stimulation. The results are discussed with reference to existing theories of reaction times.

The treatment of response times as a function of stimulation intensity appears in mathematical biology in two connections; 1) the response of a peripheral nerve to an applied potential difference, which may be constant (Blair, 1932a) or variable, as for example in a condenser discharge or in a source of an alternating current (Blair, 1932b); and 2) the response of the total organism to stimulation of its sense receptors, as in the determination of reaction times (Piéron, 1920–1921; Householder and Landahl, 1945; Rashevsky, 1948).

In the case of the peripheral nerve the simplest mathematical treatment of response time-intensity relations is that of H. A. Blair, sometimes referred to as the "one-factor theory." There it is assumed that the "excitatory factor," whatever its nature might be, is subjected to two influences, namely a tendency to accumulate at a rate proportional to the magnitude of the impressed voltage (or the current flowing through the nerve, if the resistance of the latter is assumed constant) and a tendency to dissipate at a rate proportional to its own "concentration." Hence the equation

$$\frac{d\epsilon}{dt} = A I - k\epsilon, \tag{1}$$

where ϵ is the "concentration" of the excitation factor, I, the impressed voltage (or current), A and k being constants.

It is further assumed that the nerve becomes active, i.e., the spike potential appears and begins to propagate along the nerve, when the concentration of excitation reaches a certain critical level h. Integration of equation (1) and the substitution of h for ϵ then gives the response time t^* as a function of the intensity I and the constants (the parameters of the nerve), namely

$$t^* = \frac{1}{k} \log \frac{AI}{AI - kh}, \tag{2}$$

which satisfies the conditions $t^*(h) = \infty$, $t^*(\infty) = 0$. Equation (2) gives good agreement with experimental data on the response times to a constant potential applied to peripheral nerve (Blair, 1932a).

N. Rashevsky (1948) has used a formally equivalent theory to derive the response time of an efferent neuroelement as a function of the intensity of activity in an afferent neuroelement synapsing on the former. It was found, furthermore, that if the intensity of activity in the afferent neuroelement was assumed to be a logarithmic function of the external stimulus intensity (e.g., brightness in the case of visual stimulation, concentration in the case of a gustatory stimulus, etc.) very good agreement could be obtained between the corresponding theoretical equation, relating stimulus intensity to response time, and the reaction times of human subjects to sense stimuli (Householder and Landahl, *loc. cit.*; Rashevsky, *loc. cit.*).

It thus appears that the response time-intensity relation derived from the simple assumptions of the one-factor theory (plus a logarithmic interpretation of stimulus intensity) fits the data on reaction times, where probably large sections of the nervous system are involved. It seems at first surprising that this should be so, inasmuch as only one neural connection is involved in the model where the equation of the one-factor theory is applied to the derivation of the over-all reaction time; all the more so since the magnitudes of these reaction times exceed by a factor of some hundreds the usually observed magnitudes of synaptic delays. N. Rashevsky (1948) has shown, however, in his reinterpretation of the fundamental equation in terms of large numbers of reverberating cycles, that the "single connection" can be interpreted as a "macro-synapse" with a large number of neurons, so organized that the continuous rise of excitation is a reflection of the activation of more and more cycles, while the dissipation of excitation is due to accidental de-activation of the cycles. The formal aspect of the theory is thereby preserved.

In this paper we shall propose an alternative model, also based on a

large number of neurons, each behaving in accordance with the all-or-none law, where no assumptions concerning the organization of these neurons into cycles are required. On the contrary, we shall suppose the greatest possible chaos, characteristic of a random net, where the probability of a direct connection between any pair of neurons is the same. Such a random net was described in previous papers (Solomonoff and Rapoport, 1951; Rapoport, 1951, 1952). We shall refer most often to the last mentioned paper, hereafter designated by *loc. cit.*

If, as it is reasonable to suppose, the neural events involved in reaction times of human subjects following instructions (i.e., events other than simple reflexes) depend on the activity of higher centers (e.g., the association areas of the cortex), it seems to the author advantageous to use probabilistic concepts in developing a theory of such events. For, loosely speaking, it can be conjectured that such centers are much less "rigidly" organized than the older pathways involving, say, inherent reflex responses. The functional pathways of the higher centers may well be in a state of relative flux, quickly changing with the situation to be met. That is why the postulate of a chaotic random net seems to the author a more promising approach than postulates of specific connections, specifically organized to explain a psychological phenomenon.

Accordingly we shall consider the response time of a random net of the type described in previous papers, particularly in *loc. cit.* Some of the neurons of such a net $\mathfrak{N}$ will be supposed to be stimulated from the outside, either instantaneously (just once) or continuously (once every unit of time). Quantized time is assumed throughout, the unit being the synaptic delay. Any imposed excitation may spread throughout $\mathfrak{N}$ because of the connections between the neurons of $\mathfrak{N}$. The *response time* will be defined as the time required for the activity of $\mathfrak{N}$ to reach a certain level, assumed as being the threshold of the effectors stimulated by $\mathfrak{N}$, from which effectors the behavior associated with the overt reaction to the stimulus results.

In *loc. cit.* we designated by $x(t)$ the number of neurons firing in $\mathfrak{N}$ at the (quantized) instant t. In this paper we shall consider instead $z(t) = x/N$, i.e., the fraction of neurons firing. The translation of the equations of *loc. cit.* into this notation is obvious.

Case 1. Instantaneous Stimulation; $\mathrm{h} = 1$; $\mathrm{a} > 1$. It will be recalled (cf. *loc. cit.*) that h is the individual threshold of the neurons of $\mathfrak{N}$, i.e., the number of stimuli which must impinge simultaneously upon any neuron in $\mathfrak{N}$ to elicit a firing. If each stimulus received by a neuron results in a firing, then $h = 1$. The axon density, denoted by a, is the average number

of axons sent out per neuron. In the case we are about to consider, we suppose that $h = 1$, $a > 1$ (the case $h = 1$, $a \leqq 1$ is trivial, since any initial stimulation will die out, i.e., $z = 0$ is the only steady state). As stated above, $z(t)$ is the fraction of neurons firing at the instant t. Following the reasoning of *loc. cit.*, we arrive at the equation

$$\frac{dz}{dt} = 1 - e^{-az} - z\,. \tag{3}$$

If H is the level of excitation at which response takes place* [i.e., the "over-all" threshold of the net, $H > z(0)$], then the time of response will be given by

$$t^* = \int_{z(0)}^{H} \frac{dz}{1 - e^{-az} - z}\,. \tag{4}$$

Equation (4) gives the response time-intensity curve under the conditions considered. Here $z(0)$, being the initial and only outside stimulation, rep-

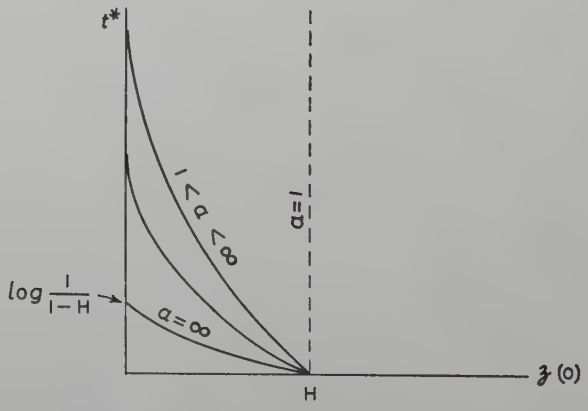

FIGURE 1. Response-time plotted against instantaneous stimulation for various values of a. The lowermost curve is the limiting case, $a = \infty$. The dotted line is the undefined case, $a = 1$.

resents the intensity, while H and a are the parameters of the net. By inspection, we see that $t^*(0) = \infty$; $t^*(H) = 0$; $dt^*/dz(0) < 0$ for all values $0 < z(0) < H$, $(a > 1)$. For very large a (negligible e^{-az}), we have the approximation

$$t^* \cong \int_{z(0)}^{H} \frac{dz}{1 - z} = \log \frac{1 - z\,(0)}{1 - H}\,, \tag{5}$$

while for a very close to 1, equation (4) becomes meaningless since the steady state approaches zero and H cannot exceed it. The family of curves for our range of a is represented in Figure 1.

* We suppose that H is less than the steady state level of activity as defined in *loc. cit.*

If $aH \ll 1$, it is easy to obtain an approximate quadrature indicated in (4) in closed form. In that case $az \ll 1$, and we can approximate e^{-az} by $1 - az$, obtaining

$$t^* \cong \int_{z(0)}^{H} \frac{dz}{z(a-1)} = \frac{1}{a-1} \log \frac{H}{z(0)}. \tag{6}$$

With a better approximation,

$$e^{-az} \cong 1 - az + \frac{a^2 z^2}{2},$$

formula (6) is corrected to

$$t^* \cong \frac{1}{a-1} \log \frac{H\left(\frac{a-1-a^2H}{2}\right)}{z(0)\left[\frac{a-1-a^2 z(0)}{2}\right]}. \tag{7}$$

Any desired approximation can be obtained by expanding the integrand of (4) in series. We first expand the denominator getting

$$\begin{aligned} 1 - e^{-az} - z &= z(a-1) + \sum_{j=2}^{\infty} \frac{(-1)^{j-1}(az)^j}{j!} \\ &= z\left[(a-1) + \sum_{j=1}^{\infty} \frac{(-1)^j a^{j+1} z^j}{j+1}\right]. \end{aligned} \tag{8}$$

The series within the brackets of (8), being analytic at $z = 0$, can be inverted. Its reciprocal is

$$\frac{1}{a-1} + \frac{a^2}{2(a-1)^2} z + \frac{a^4 + 2a^3}{12(a-1)^3} z^2 + \ldots. \tag{9}$$

Hence the entire reciprocal of the integrand is

$$\frac{1}{(a-1)z} + \frac{a^2}{2(a-1)^2} + \frac{a^4 + 2a^3}{12(a-1)^3} z + \ldots, \tag{10}$$

which, integrated termwise, gives us the expression for t^* as a series in $z(0)$ and H, namely

$$t^* = \frac{1}{a-1}\left\{\log \frac{H}{z(0)} + \frac{a^2}{2(a-1)}[H - z(0)] + \frac{a^4 + 2a^3}{24(a-1)^2}[H^2 - z^2(0)] + \ldots\right\}.$$

This series converges quite rapidly if a is not too large, i.e., $aH < 1$.

Case 2. Continuous Stimulation. Now let f be the fraction of neurons per unit time in $\mathfrak{N}$ constantly stimulated by an outside source. Hence f is a measure of the intensity of that stimulation. Pick a neuron of $\mathfrak{N}$ at ran-

dom. Consider the probability that at time $t + 1$ it is stimulated neither by the outside source nor by any of the neurons within $\mathfrak{N}$ [of which there were $x(t)$ active at time t, i.e., having $ax(t) = Naz(t)$ active axones]. This probability is given by the product

$$(1 - f)\ e^{-az(t)}\ . \tag{11}$$

The first factor is the probability of not being stimulated by the outside source; the second, the probability of not being stimulated by a neuron of $\mathfrak{N}$. The two events are assumed independent. Therefore the probability of being stimulated by either source at the time $t + 1$ will be

$$1 - (1 - f)\ e^{-az}\ , \tag{12}$$

and our differential equation for the spread of excitation becomes

$$\frac{dz}{dt} = 1 - (1 - f)\ e^{-az} - z\ . \tag{13}$$

The reaction time will accordingly be given by

$$t^* = \int_0^H \frac{dz}{1 - (1 - f)\ e^{-az} - z}\ . \tag{14}$$

Of particular interest is the case when $a < 1$, $H \ll 1$. We recall that this case was trivial under the condition of instantaneous stimulation, because there the excitation simply died out, whatever was the outside stimulation. Here, however, excitation is constantly "fed" into our net. If H (and consequently the range of z) is so small that all but the linear terms may be neglected, equation (14) becomes upon integration

$$t^* = \frac{1}{1 - a} \log \frac{f}{f - (1 - a)\ H}\ , \tag{15}$$

which is of exactly the same form as the "classical" equation (2) with $AI = f$ (the activity of the afferent); $1 - a = k$ (the rate of "dissipation" of the excitation) and $H = h$ (the threshold of the efferent).

With a proper interpretation of f as a function of the intensity of the outside stimulus, we have here a random net model of the reaction-time theory.

The condition $a < 1$ becomes particularly interesting if one allows oneself a little speculation. In our random net, a is the axon density of the net. Small a ($a < 1$) means that on the average less than one axon is emitted per neuron. Anatomically speaking, this assumption is quite improbable, since it postulates the existence of neurons without axons. Functionally

speaking, however, the interpretation is different. Our "net" is not necessarily a geographically determined collection of neurons. It is rather a functionally determined collection which becomes functionally significant in a *given situation* (for example the subject's attention being fixed on the requirements of the experiment). Hence our net may be a *selected* collection of neurons which will participate in a given task. In such a collection, the axon density may well be less than unity. *With practice*, certain neurons may be functionally eliminated from the collection and certain others added with a resulting increase in the axon density and a corresponding reduction in reaction time. We note from Figure 1 that this reduction is most pronounced (in the case of instantaneous stimulation) at small values of $z(0)$, indicating greater "sensitivity" to proper stimulation. Similar effects may be derived from the assumption of continuous stimulation.

Case 3. h $>$ *1.* We have seen (*loc. cit.*) that, for $h > 1$ and under the assumption of quantized time, excitation in a random net started by an instantaneous stimulation propagates according to the following equation:

$$\frac{dz}{dt} = 1 - e^{-az} E_{h-1}(az) - z \tag{16}$$

where

$$E_k(y) = \sum_{j=0}^{k} \frac{y^j}{j!}.$$

The corresponding response time will be

$$t^* = \int_{z(0)}^{H} \frac{dz}{1 - e^{-az} E_{h-1}(az) - z}. \tag{17}$$

We have also seen that random nets with $h > 1$ exhibit the "ignition phenomenon," that is, the initial excitation of a certain minimum number of neurons will result in a further spread of the excitation toward a stable steady state, whereas the excitation of a number of neurons less than the minimum will die out. This "ignition phenomenon" is reminiscent of a threshold. However, the notion of threshold in peripheral nerve excitation is usually connected with a minimum applied voltage sufficient to excite. Analogous to this notion would be the continuous stimulation of a constant fraction of neurons.

Let f be that fraction. Then, following the same reasoning as that preceding equation (9), we obtain the modified form of equation (16), namely

$$\frac{dz}{dt} = 1 - (1 - f)\, e^{-az} E_{h-1}(az) - z. \tag{18}$$

The proof of the existence of the ignition phenomenon in *loc. cit.* proceeded by a semi-quantitative argument. It will be recalled that we superimposed the graphs of $1 - z$ and of

$$e^{-az}E_{h-1}(az)$$

against z over each other, and showed that, for sufficiently large values of a, the line $1 - z$ intersects the curve

$$e^{-az}E_{h-1}(az)$$

in two points, $z = \beta_1$ and $z = \gamma_2$, the two steady states of z. We further showed that γ_1, the smaller value, was an unstable state, and γ_2 a stable

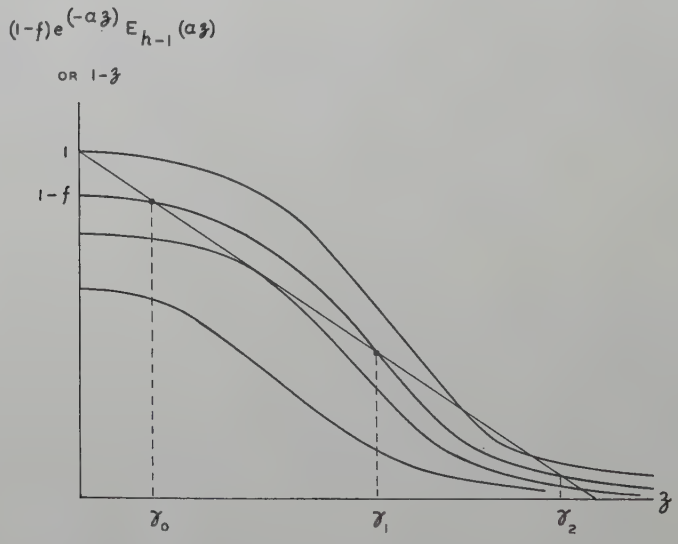

FIGURE 2. The line $1 - z$ and the family

$$(1 - f)e^{-az}E_{h-1}(az)$$

plotted against z for various values of f. The uppermost curve is for $f = 0$. The next curve is for $f < H$. The tangent curve is for $f = H$, and lowermost for $f > H$.

one, so that the excitation starting with $z < \gamma_1$ would tend to die out, while one starting with $z > \gamma_1$ would tend toward γ_2. The reader is referred to Figure 1 of *loc. cit.*

Let us now apply similar considerations to the right side of (18). We hold a fixed at a sufficiently large value so that for $f = 0$ there are two intersections. Consider now a family of curves corresponding to increasing values of the parameter f, which, we recall, is a measure of the intensity of the outside stimulus. This family is shown in Figure 2.

As we increase f, the factor $(1 - f)$ of the expression

$$(1 - f)\ e^{-az}E_{h-1}(az)$$

decreases. Thus the entire curve is depressed. There is a critical value $f^* = H$ for which the curve is tangent to the line $1 - z$. This critical value, we maintain, is the threshold of the net $\mathfrak{N}$ under continuous stimulation.

To establish this, we must show that for $f < H$, the initial fraction of neurons stimulated is less than γ_1 (the unstable steady state) and remains so, otherwise the excitation will tend toward γ_2. That this is so follows from the fact that the derivative with respect to z of

$$(1 - f)\ e^{-az}E_{h-1}(az)$$

is always negative for $z > 0$, as can be verified by direct differentiation.

This implies that the ordinate of any point on the curve is less than the ordinate of the starting point (where $z = 0$). If $f < H$, there are three intersections of the curve with the line $1 - z$ corresponding to values γ_0, γ_1, and γ_2 of z. Therefore the ordinate of γ_0 is $1 - \gamma_0$, and this is less than the ordinate at $z = 0$, namely $1 - f$. Then

$$1 - \gamma_0 < 1 - f \qquad \text{or} \qquad f < \gamma_0 . \tag{19}$$

Hence, *a forteriori*, $f < \gamma_1$, and our contention is proven with respect to the initial stimulation. That excitation in this case will tend toward $\gamma_0 < \gamma_1$ follows from the fact that at $z < \gamma_0$, $dz/dt > 0$ and at $z > \gamma_0$, $dz/dt < 0$. Therefore γ_0 is a stable state. Therefore, for any subthreshold stimulation $f < H$, excitation will at first grow until it is stabilized about γ_0, a nonzero steady state.

For $f = H$, $\gamma_0 = \gamma_1$ becomes an unstable steady state, and the excitation will spread to the next stable steady state γ_2. For any value $f > H$, there is only one steady state, namely, γ_2. The evaluation of the threshold H can be obtained from the following

Theorem. Let h > 1 *be the individual neuron threshold in a random net* $\mathfrak{N}$, *whose axon density is sufficiently large to give non-zero steady states. Then the over-all net threshold* H *with respect to a constant stimulation* f *is given by the simultaneous solution of the following equations:*

$$1 - (1 - f)\ e^{-az}E_{h-1}(az) - z = 0 , \tag{20}$$

$$a(1 - f)\ e^{-az}\frac{a^{h-1}z^{h-1}}{(h-1)!} - 1 = 0 . \tag{21}$$

Proof. Equation (20) determines the intersections of the curve

$$(1 - f)\ e^{-az}E_{h-1}(az)$$

with the line $1 - z$, and hence the steady states. Equation (21) is obtained by setting the derivative of

$$(1 - f)\, e^{-az} E_{h-1}(a z)$$

equal to -1. The two equations together are the conditions for tangency between the curve and the line, in which case $\gamma_0 = \gamma_1$, i.e., $f = H$.

Remark. It must be kept in mind that all our considerations are probabilistic. It is not *certain* that a subthreshold stimulation results in the excitation always staying below γ_0. This value is only a theoretically deduced steady state. Actual excitation may fluctuate around it, being sometimes above and sometimes below. Now if γ_0 and γ_1 are close together, i.e., f is subthreshold but close to the threshold, it may happen that a fluctuation of z may carry it beyond γ_1, and an "explosion" toward γ_2 may result. We have here a model for over-all threshold fluctuations, even though the individual neuron thresholds are fixed at $h = 1$. It would be interesting to compute the form of these fluctuations, for example, to determine if they are normally distributed.

Conclusions. We have shown how a theory of reaction times can be derived on the basis of a "discontinuous" theory of neural action without postulating anything about the structure of an aggregate of neurons other than the condition of "chaos."

In a very special case, the equation deduced from the random net theory reduces to the "classical" equation derived from the application of the one-factor theory to a single connection. Hence the random net equations are a generalization of the one-factor theory equations. However, the most interesting theoretical result of the random net theory of reaction times is that it implies a quantitative relation between the thresholds of stimulation for two methods of stimulation—by a short (flash) stimulus and by a continuous (constant) stimulus. The former threshold can be computed from equations (20) and (21). The latter threshold is the smaller root of equation (21) of *loc. cit.* For fixed parameters of a given net (i.e., a and h), it is easily seen that the threshold of continuous stimulation is always smaller than the threshold of flash stimulation. This result finds qualitative experimental verification (Piéron, *loc. cit.*, Geblewitz, 1935).

Furthermore a quantitative relation is implied between the respective reaction times for the cases of super threshold flash stimulations and continuous stimulations of equal intensity. The former is given by equation (17); the latter can be obtained analogously from equation (18). Even if the continuous stimulation is a given function of time $f(t)$, the reaction

time can, in principle, be calculated from equation (18). These additional relations provide a possibility of reducing the number of unknown parameters in the reaction time equation.

One is tempted to apply these theoretical results to available data on reaction times. A wealth of such data, especially relating to the comparison of reaction times for continuous and flash stimulation is found in the work of Piéron and his school (Piéron, *loc. cit.*). It appears, however, that such applications cannot be made without a rather thoroughgoing analysis.

To begin with, Piéron's scale of stimulation intensities is not in terms of some objective unit but in multiples of threshold stimulation. Since the thresholds for the two methods of stimulation are widely different, the data must be reinterpreted in objective (energy) units.

The second difficulty is more serious. The wide variations of reaction times for various modalities of sensation indicate that perhaps very different classes of events are operating in each case. What is measured in any reaction time experiment is the time interval between the activation of the stimulation source and a previously agreed upon response in the subject (in the case of human subjects, the pressing of a key). During this time, the following events presumably occur: 1) the passage of energy from the source to the receptors of the subject; 2) the activation of the receptors; 3) the passage of impulses along the neural pathways of the subject; 4) the contraction of appropriate muscles which constitute the response.

Strictly speaking, a theory which deduces a quantitative relation between the intensity of the stimulus and reaction time must relate the intensity to the time course of events in each of the above mentioned phases. The usual practice is to lump three of those levels into a constant and to deduce the intensity-reaction time relation in terms of the remaining one. This is implied in one of the earliest theories of reaction time, namely, that deducible from the so-called Bloch's Law, which postulates a simple reciprocal relation between intensity and the time necessary to excite (constant "dose"). Here the variable factors are by implication attributed to the events at the *receptors*, all the other events (including those in the central nervous system) being considered constant.

On the other hand the Landahl theory (Householder and Landahl, *loc. cit.*) considers the variable component to be the events at a connection between an afferent and an efferent neural pathway and lumps into a constant the time passing in the activation of the receptors and in what occurs after the excitation has crossed the connection.

Piéron (*loc. cit.*) attempts to consider both the activation of the recep-

tors and the neural events as variable, but the latter are not treated with mathematical rigor for want of a suitable theoretical model.

It appears that three rather different theories yield similarly shaped curves relating intensity of stimulation to reaction time. Piéron's theory is essentially a modification of Bloch's Law. It focuses attention on the activation time of the receptors. The Landahl theory is an application of Blair's one-factor theory to a neural connection together with an assumption of a logarithmic relation between the objective intensity of the stimulus and the activity in a neural pathway. The random net theory assumes a spread of excitation through an aggregate of neurons randomly connected and interacting "digitally," i.e., in accordance with the discontinuous model of the central nervous system of McCulloch and Pitts (1943). The similarity of the intensity-reaction time curves deduced from the three theories makes it possible to fit the observed data to any one of them. To compare the relative merits of the theories, one must therefore go beyond curve fitting—one must find suitable interpretations of the parameters involved and devise means of varying these parameters in an experimental situation. This leads to questions concerning the relative importance of the different phases of activity listed above in the interpretation of the reaction time curve. It is noteworthy, for example, that the reaction times for certain modalities of stimulation are much larger than others. For example, in thermal stimulation of the human skin (Geblewitz, *loc. cit.*) the response for continuous stimulation are of the order of one second, approaching asymptotically the minimal value of 0.3 to 0.4 seconds. For gustatory stimulation (Piéron, *loc. cit.*) the response times in the vicinity of the threshold are of the order of 2 to 3 seconds, approaching the minimal value of 0.25 seconds. Experiments on invertebrates have shown responses to light stimuli delayed as long as 7 seconds (Hecht, *loc. cit.*). Responses to visual stimuli, on the other hand, are usually in the vicinity of 0.3 seconds in the threshold neighborhood and approach values of less than 0.2 minimally (Piéron, *loc. cit.*).

These wide variations indicate that many different mechanisms may be responsible for the intensity-response time relation. Any refinement of the existing theories, therefore, must take some such possible mechanisms into account. In the case of thermal stimulation, it would be interesting to consider the quantitative relation between the intensity of stimulation and the time necessary for the energy of stimulation to penetrate the epidermis to the receptors. In the case of gustatory stimulation, the same problem presents itself in connection with the diffusion of the chemical stimulant throughout the region where the receptors are situated. This

latter problem is especially interesting inasmuch as different chemicals give different reaction time curves.

Some of the considerations outlined here will be treated in subsequent papers.

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THE SMALLEST VALUE OF THE AXON DENSITY FOR WHICH 'IGNITION' CAN OCCUR IN A RANDOM NET

ERNESTO TRUCCO
COMMITTEE ON MATHEMATICAL BIOLOGY
THE UNIVERSITY OF CHICAGO

As shown by A. Rapoport (1952), when a very brief stimulation or "instantaneous input" is applied to a random net, the subsequent events are determined by the parameters of the net as follows: If the axon density a is sufficiently large and the fraction γ of the neurons initially stimulated exceeds a certain value γ_1 (the *over-all* threshold of the net for instantaneous stimulation), excitation will spread through the net until a steady state is reached in which a fraction $\gamma_2 \geqslant \gamma_1$ of the neurons is firing ("ignition phenomenon"). If $\gamma < \gamma_1$ the activity in the net dies out. However, if the axon density is too small, the activity will ultimately die out, no matter how large the fraction of initially stimulated neurons. Thus there exists a limiting value A of the axon density below which the net cannot "ignite." This A is a function of h, the *individual* threshold of the neurons constituting the net (we assume here $h \geqslant 2$, since for $h=1$ the situation is essentially different). Geometrically γ_1 and γ_2 are determined as the two intersection points of a straight line with a sigmoid curve. When $a < A$ the two curves do not intersect and for $a = A$ they are tangent.

In this paper the "tangency case" is investigated and the general features of the function $A(h)$ are determined. It is shown that A increases monotonically with h (as one would expect). For all values of $h > 1$ we have $A(h) > h$, but the fraction $A(h)/h$ and the derivative $dA(h)/dh$ approach unity as h increases. An analytical expression of the function $A(h)$ valid for very large values of h is derived.

Consider a random net $\mathfrak{N}$ as described by Rapoport (*loc. cit.*). Upon being fed an initial instantaneous input, the net can reach a positive steady state only if

$$1 - e^{-a\gamma} E_{h-1}(a\gamma) - \gamma = 0 \tag{1}$$

[Rapoport, equation (20)].

Here γ is the fraction of neurons firing steadily, a is the axon density (average number of axons emitted by each neuron) and h (an integer) the individual threshold, assumed equal for all neurons.

For a given $h > 1$, equation (1) has no real solution γ if a is smaller than a certain number A (which we wish to determine), whereas if $a > A$ equa-

tion (1) has two distinct solutions γ_1 and γ_2. This is seen by plotting the two functions

$$\varphi(\gamma) = 1 - \gamma$$

and

$$\psi(\gamma) = e^{-a\gamma} E_{h-1}(a\gamma)$$

vs. γ (Fig. 1; also Fig. 1 in Rapoport).

For $a = A$ the two curves $\varphi(\gamma)$ and $\psi(\gamma)$ are tangent, i.e., we have:

$$1 - \gamma = e^{-A\gamma} E_{h-1}(A\gamma), \tag{2}$$

$$-1 = -A\, e^{-A\gamma} \frac{(A\gamma)^{h-1}}{(h-1)!}. \tag{3}$$

By eliminating γ from (2) and (3) we obtain a relation between A and

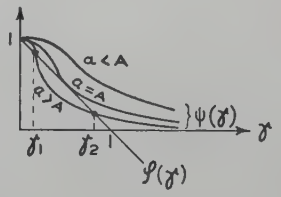

FIGURE 1

h, giving us the minimum value of the axon density for which the net will still "ignite" as a function of the individual threshold.

If we put

$$A\gamma = y \tag{4}$$

equations (2) and (3) become:

$$1 - y\frac{1}{A} = e^{-y} E_{h-1}(y), \tag{5}$$

$$\frac{1}{A} = e^{-y} \frac{y^{h-1}}{(h-1)!}. \tag{6}$$

Inserting (6) into (5) we obtain an equation involving only h and y:

$$1 - e^{-y} E_{h-1}(y) = \frac{e^{-y} y^h}{(h-1)!}. \tag{7}$$

This last equation implicitly defines a function $y = f(h)$, which, when substituted into (6), will show how A depends on h.

It is easy to solve equation (7) by trial and error for small values of h. We have, e.g., for $h = 2$:

$$1 - e^{-y}[1 + y] = e^{-y} y^2,$$

which is satisfied for $y = 1.79\ldots \equiv y(2)$. We then find from (6) that $A(2) = 3.34\ldots$.

Similarly, for $h = 3$ equation (7) becomes

$$1 - e^{-y}\left[1 + y + \frac{y^2}{2}\right] = \frac{e^{-y}y^3}{2},$$

which gives us $y(3) = 3.38\ldots$ and $A(3) = 5.14\ldots$.

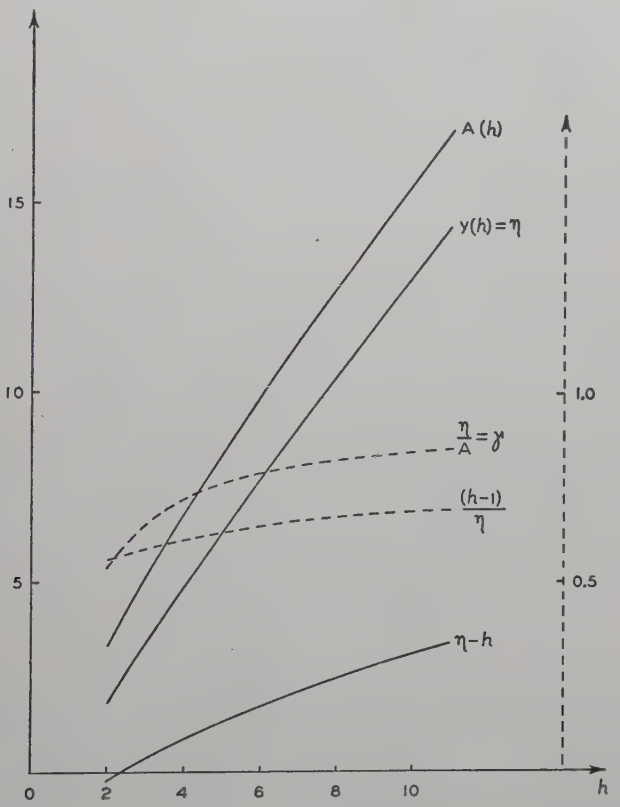

FIGURE 2. Ordinates at right refer to dash-lined curves, ordinates at left to full-drawn curves.

Figure 2 shows the graphs of $y(h)$ and $A(h)$ calculated in this way for values of h ranging between 2 and 11. (Numerical data are collected in Table I.)

However, to obtain a complete picture of the function $A(h)$ it is necessary to study the behavior of equation (7) for very large values of h.

Putting

$$G_h(y) \equiv 1 - e^{-y}E_{h-1}(y), \tag{8}$$

we notice that

$$G_h(y) = \frac{1}{(h-1)!}\int_0^y e^{-t}t^{h-1}dt. \tag{9}$$

Equation (9) can be shown by induction or, more directly, by verifying that

$$\frac{dG_h(y)}{dv} = e^{-y}\frac{y^{h-1}}{(h-1)!} \quad \text{and} \quad G_h(0) = 0.$$

TABLE I

h	$y(h)\equiv\eta$	$A(h)$	$\eta-h$	$(h-1)/\eta$	$\eta/A\equiv\gamma$	$A(h)$ calculated from equation (50)
2.....	1.79	3.34	−0.21	0.56	0.54	.....
3.....	3.38	5.14	0.38	0.59	0.66	.....
4.....	4.88	6.80	0.88	0.61	0.72	.....
5.....	6.32	8.36	1.32	0.63	0.76	.....
6.....	7.72	9.86	1.72	0.65	0.78	.....
8.....	10.45	12.79	2.45	0.67	0.82	9.47
11.....	14.39	16.93	3.39	0.69	0.85	13.67

Equation (7) now becomes:

$$\frac{e^y}{y^h}\int_0^y e^{-t}t^{h-1}dt = 1, \tag{10}$$

or, introducing the new variable of integration, $u = 1 - (t/y)$,

$$H_h(y) \equiv \int_0^1 e^{uy}(1-u)^{h-1}du = 1. \tag{11}$$

It may be of interest for future calculations to notice that the integral in (10) is the incomplete Γ-function $\gamma(h, y)$ (in the notation of Whittaker & Watson, 1945, p. 341), whereas for the integral in (11) we have:

$$H_h(y) = \frac{1}{h}\cdot F[1, (h+1); y], \tag{12}$$

where

$$F[1,(h+1);y] = 1+\frac{y}{(h+1)}+\frac{y^2}{(h+1)(h+2)} + \frac{y^3}{(h+1)(h+2)(h+3)}+\cdots$$

is the well-known confluent hypergeometric series.*

Equation (7) has only one solution $y(h) \neq 0$ ($y = 0$ being a trivial solution). This can most easily be seen from (11). We have:

$$\frac{dH_h(y)}{dy} = \int_0^1 e^{uy}(1-u)^{h-1}u\,du > 0\,. \tag{13}$$

Thus, $H_h(y)$ and $dH_h(y)/dy$ are monotonically increasing functions of y. Also:

$$\left.\begin{aligned} H_h(0) &= \frac{1}{h} < 1 \quad \text{if} \quad h > 1\,, \\ \left[\frac{dH_h(y)}{dy}\right]_{y=0} &= \frac{1}{h(h+1)} > 0\,, \end{aligned}\right\} \tag{14}$$

and, for any fixed value of y,

$$\left.\begin{aligned} H_{h+1}(y) &< H_h(y)\,, \\ \frac{dH_{h+1}(y)}{dy} &< \frac{dH_h(y)}{dy}\,. \end{aligned}\right\} \tag{15}$$

Plotting the family of curves $H_h(y)$ vs. y (Fig. 3), we therefore see that any of them intersects the horizontal line of height 1 in one point only. Moreover, $y(h)$ increases monotonically with h.

We also plot the functions $G_h(y)$, (8), and

$$M_h(y) = \frac{e^{-y}y^h}{(h-1)!} \tag{16}$$

vs. y (Fig. 4). Equation (10) can be written:

$$G_h(y) = M_h(y)\,. \tag{17}$$

* In general:

$$F(a,\gamma;y) = \sum_{\nu=0}^{\infty}\frac{\Gamma(\gamma)\,\Gamma(a+\nu)}{\Gamma(a)\,\Gamma(\gamma+\nu)}\frac{y^\nu}{\nu!} = \frac{\Gamma(\gamma)}{\Gamma(\gamma-a)\,\Gamma(a)}\int_0^1 e^{uy}(1-u)^{\gamma-a-1}u^{a-1}du\,,$$

$$F(a,\gamma;0) = 1\,,$$

$$\left[\frac{\partial}{\partial y}F(a,\gamma;y)\right]_{y=0} = \frac{a}{\gamma}\,.$$

Now, $G_h(y)$ remains less than 1 and tends to 1 for $y \to \infty$, whereas $M_h(y)$ has a maximum at $y = h$ and becomes equal to 0 for large y's. Using Stirling's approximation,

$$e^{-h}h^h \cong (h-1)!\sqrt{\frac{h}{2\pi}}, \tag{18}$$

we find:

$$M_h(h) \cong \sqrt{\frac{h}{2\pi}}. \tag{19}$$

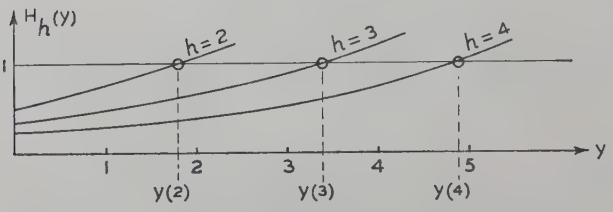

FIGURE 3

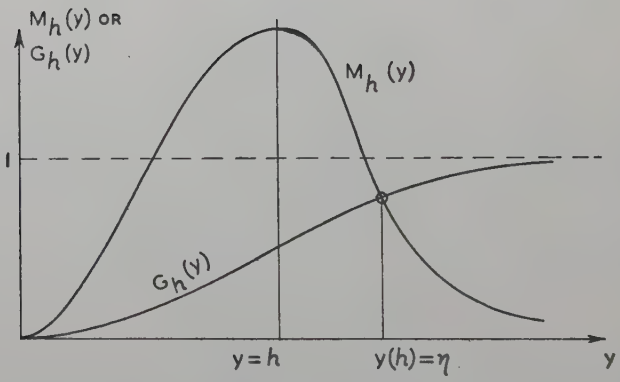

FIGURE 4. Not on scale

This shows that

$$y(h) > h \tag{20}$$

if h is sufficiently large.*

In what follows we shall denote by $\eta\ [=y(h)]$ that particular value of y which satisfies equation (7) for a given h. Then, multiplying (7) by $\exp(\eta - h)$ and using (19) and (20), we obtain:

$$e^{\eta-h} = e^{-h}E_{h-1}(\eta) + \frac{e^{-h}\eta^h}{(h-1)!} > \frac{e^{-h}h^h}{(h-1)!} \approx \sqrt{\frac{h}{2\pi}}.$$

* Actually (20) holds for $h > 2$ (see Fig. 2).

Hence:

$$\eta - h > \tfrac{1}{2} \ln\left(\frac{h}{2\pi}\right), \tag{21}$$

$$\frac{\eta}{h} > 1 + \frac{1}{2h} \ln\left(\frac{h}{2\pi}\right). \tag{22}$$

Since $y(h)$ increases with h and $G_h(y)$ tends to 1 for $y \to \infty$, we would expect that for large h's equation (10) or (17) should be equivalent to

$$M_h(y) = \frac{e^{-y} y^h}{(h-1)!} = 1. \tag{23}$$

This can be shown rigorously as follows. Multiplying equation (7) by $[1/M_h(\eta)]$ we find:

$$\frac{(h-1)!}{e^{-\eta}\eta^h} = 1 + \Phi(\eta)$$

where

$$\Phi(\eta) = \frac{(h-1)!}{\eta^h} E_{h-1}(\eta).$$

For an arbitrarily large but fixed h we then have, since $(h-1)/\eta < 1$,

$$\Phi(\eta) = \frac{(h-1)!}{\eta^h} \sum_{\nu=0}^{h-1} \frac{\eta^\nu}{\nu!} = \frac{1}{\eta} \sum_{\mu=0}^{h-1} \frac{(h-1)!}{(h-1-\mu)!} \eta^{-\mu}$$

$$< \frac{1}{\eta} \sum_{\mu=0}^{h-1} \left(\frac{h-1}{\eta}\right)^\mu < \frac{1}{(\eta - h + 1)}.$$

Using (21) we therefore conclude that $\Phi(\eta)$ becomes negligibly small with increasing h and this proves our assertion.

Now consider equation (23). Again using Stirling's formula (18) we can write

$$M_h(y) \cong \sqrt{\frac{h}{2\pi}}\, e^{-(y-h)} \left(\frac{y}{h}\right)^h. \tag{24}$$

If we put $y = a \cdot h$ in (24) (a being a real number greater than 1 and independent of h), we obtain:

$$M_h(ah) \cong \sqrt{\frac{h}{2\pi}}\, \rho^h,$$

where

$$\rho = \frac{a}{e^{a-1}} < 1 \qquad \text{if} \qquad a > 1.$$

Since for $\rho < 1$ the quantity $\sqrt{(h/2\pi)}\, \rho^h$ tends to zero as $h \to \infty$, we must have $\eta < ah$, or

$$\frac{\eta}{h} < a \qquad \text{for} \qquad h \to \infty. \tag{25}$$

Inequality (25) can be made to hold for any value of $\alpha > 1$, no matter how near to 1, provided only h is chosen large enough. Comparing with (20) or (22) we conclude that:

$$\frac{\eta}{h} \xrightarrow[(h\to\infty)]{} 1 . \tag{26}$$

If h be considered as a continuous variable we can use these results to study the derivative $dy(h)/dh$. Putting:

$$\frac{\partial H_h(y)}{\partial y} = \int_0^1 e^{uy}(1-u)^{h-1}u\,du \equiv K_h(y) > 0 \tag{27}$$

$$\frac{\partial H_h(y)}{\partial h} = \int_0^1 e^{uy}(1-u)^{h-1}\ln(1-u)\,du \equiv L_h(y) < 0 , \tag{28}$$

we have:

$$y' \equiv \frac{dy(h)}{dh} = -\frac{L_h(\eta)}{K_h(\eta)} . \tag{29}$$

Since $-\ln(1-u) > u$ (for $0 < u < 1$), it follows that

$$y' > 1 . \tag{30}$$

On the other hand, integration by parts yields the formula:

$$H_{h+1}(y) = -\frac{1}{y} + \frac{h}{y} \cdot H_h(y) \tag{31}$$

or, replacing h by $(h-1)$,

$$H_h(y) = -\frac{1}{y} + \frac{1}{y} \cdot (h-1) \cdot H_{h-1}(y) . \tag{32}$$

If $y = \eta$, so that $H_h(\eta) = 1$, we obtain from (31) and (32):

$$H_{h+1}(\eta) = \frac{(h-1)}{\eta} \tag{33}$$

and

$$H_{h-1}(\eta) = \frac{(\eta+1)}{(h-1)} . \tag{34}$$

Now, since (for $0 < u < 1$) $-(1-u) \cdot \ln(1-u) < 1-(1-u)$, we have:

$$-L_h(\eta) < H_{h-1}(\eta) - H_h(\eta) = \frac{(\eta-h+2)}{(h-1)} . \tag{35}$$

Furthermore:

$$K_h(\eta) = H_h(\eta) - H_{h+1}(\eta) = \frac{(\eta-h+1)}{\eta} . \tag{36}$$

Hence, from (29), (35), and (36):

$$1 < y' < \frac{(\eta-h+2)}{(\eta-h+1)} \frac{\eta}{(h-1)} \xrightarrow[(h\to\infty)]{} 1 . \tag{37}$$

This shows that:

$$\lim_{(h\to\infty)} \frac{dy(h)}{dh} = 1 . \tag{38}$$

It is clear that all the relations found so far will be satisfied if we assume that $y(l)$ be of the form:

$$y(h) = h + \epsilon(h) ,$$

where $\epsilon(h)$ is a function tending to infinity with h less rapidly than h itself, i.e.,

$$\lim_{(h\to\infty)} \epsilon(h) = \infty .$$

but

$$\lim_{(h\to\infty)} \frac{\epsilon(h)}{h} = 0 \qquad \text{and also} \qquad \lim_{(h\to\infty)} \frac{d\epsilon(h)}{dh} = 0 .$$

Going back to equation (23) and always assuming h to be a large number, we put:

$$\nu = h + \epsilon \tag{39}$$

and

$$\frac{\epsilon}{h} \equiv \sigma \ (\ll 1) . \tag{40}$$

Then, using Stirling's approximation once again, (23) becomes:

$$e^{-\epsilon}[1+\sigma]^h = \sqrt{\frac{2\pi}{h}} , \tag{41}$$

or, putting

$$c \equiv \sqrt{\frac{1}{h} \ln\left(\frac{h}{2\pi}\right)} \ (\ll 1) \tag{42}$$

and expanding the left-hand side of (41):

$$e^{-\epsilon}[1+\sigma]^h = e^{h[-(1/2)\sigma^2+(1/3)\sigma^3-(1/4)\sigma^4+-\ldots]} , \tag{43}$$

$$\frac{\sigma^2}{2} - \frac{\sigma^3}{3} + \frac{\sigma^4}{4} - + \ldots = \frac{c^2}{2} . \tag{44}$$

If in (44) we neglect all powers of σ higher than σ^2, we find:

$$\sigma \approx c . \tag{45}$$

which means:

$$\epsilon(h) \cong \sqrt{h \ln\left(\frac{h}{2\pi}\right)} . \tag{46}$$

Going one step further we obtain the equation

$$\frac{\sigma^2}{2} - \frac{\sigma^3}{3} = \frac{c^2}{2} , \tag{47}$$

whose solution (correct to the order c^2) is:

$$\sigma \approx c + \tfrac{1}{3} c^2 . \tag{48}$$

Therefore a better approximation for $\epsilon(h)$ will be:

$$\epsilon(h) = \sqrt{h \ln\left(\frac{h}{2\pi}\right)} + \tfrac{1}{3} \ln\left(\frac{h}{2\pi}\right). \tag{49}$$

For large h's the second term in the right-hand side of (49), though still becoming infinite with h, is nevertheless much smaller than $\sqrt{h \ln(h/2\pi)}$. The third term in (49) would be of the order $h \cdot c^3$ and therefore negligible.

Finally, having replaced equation (7) by (23) and comparing the latter with (6) we see that $A(h) \cong y(h)$, or:

$$A(h) \approx h + \sqrt{h \ln\left(\frac{h}{2\pi}\right)} + \tfrac{1}{3} \ln\left(\frac{h}{2\pi}\right) \qquad (h \gg 1). \tag{50}$$

Equation (50) gives a much more precise relation than Rapoport's crude estimate

$$A(h) > \sqrt{2\pi(h-1)}$$

[*loc. cit.*, (28)]. Unfortunately, however, it is not a very good approximation for values of h which are only moderately large (and which are likely to be of greatest interest). Thus for $h = 11$ the true value of A is 16.93, whereas equation (50) gives $A = 13.67$ (relative error $\sim 20\%$).*

Nevertheless, the foregoing considerations are sufficient to show the general behavior of the function $A(h)$. As a main result we find: The ignition phenomenon will not take place unless the axon density is larger than the individual threshold (although A and h are of the same order of magnitude). Also if $a = A$ and ignition occurs, the fraction $\gamma = y(h)/A(h)$ of neurons firing tends to 1 for large values of h.

LITERATURE

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* By far the largest part of this error comes from the fact that we solved equation (23) instead of equation (7), neglecting the term $e^{-y}E_{h-1}(y)$ in the latter. This term, as we have seen, becomes negligible for large values of h, but is relatively important if h is small. Actually, equation (49) [which is obtained from (23) by using Stirling's approximation] gives a very good approximate solution of equation (23) even for small h's, provided of course that $(h/2\pi) > 1$. Thus, the exact solution of (23) for $h = 11$ is $y = 13.63$, which differs but very little from the value given by (49), namely, $y = 13.67$.

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ON THE MATHEMATICAL THEORY OF RUMOR SPREAD

ANATOL RAPOPORT AND LIONEL I. REBHUN
COMMITTEE ON MATHEMATICAL BIOLOGY
THE UNIVERSITY OF CHICAGO

The applicability of the theory of random nets to the theory of rumor spread is shown. In particular the "weak connectivity" of the net appears as the saturation fraction of "knowers" in a thoroughly mixed population through which a message diffuses, where each knower tells the message to a finite average number of individuals. Further it is shown how the time course equation of rumor spread, where time is measured by the number of "removes" from the starters, can be translated into an ordinary continuous time course equation if the distribution of the telling intervals is known.

R. Solomonoff and A. Rapoport (1951) have defined a random net as an aggregate of points connected by directed line segments, such that the probability that a connecting link exists between a given pair of points is the same for all pairs. They have defined the "weak connectivity" of the net as the probability that a chain of connecting links exists between an arbitrary pair of points. If the total number of points approaches infinity, and if the average number of links issuing from each point is a, then, as Solomonoff and Rapoport have shown, the weak connectivity of the net is given by the single non-negative root γ of the transcendental equation

$$z = 1 - e^{-az} . \tag{1}$$

The method used by Solomonoff and Rapoport consisted of "tracing" the links issuing from an arbitrary point to the expected number of points to which they led, then tracing the links issuing from these to the expected number of *newly* contacted points, etc.

Recent experiments conducted by the Washington Public Opinion Laboratory (1952) on the spread of a message through a population followed exactly the same procedure. The points of departure were the "starters" of the message. From them the connecting links led to the "knowers once removed," from these again to the "knowers twice removed," etc. If the population is "thoroughly mixed," i.e., if the proba-

bility of transmitting the message from one individual to another is the same for each pair of individuals, one of whom is a "knower" and the other a "non-knower," then the random net is a suitable mathematical model for a theory of rumor spread, provided that the time is measured not in ordinary units (hours, days, etc.) but by the number of removes from the original knowers.

In the paper by Solomonoff and Rapoport it is tacitly assumed that there is exactly one starter (original knower). As will be presently shown, their result is easily generalizable to the cases where the number of starters is arbitrary. If one speaks of fractions of the population instead of numbers of individuals, then the assumption made by Solomonoff and Rapoport is that the fraction of starters is arbitrarily small. We shall generalize to the case in which this fraction is finite.

Of interest in the theory of rumor spread is the time course of the rumor which in the random net model appears as the expected number of points contacted in all at each remove (i.e., at each step in the tracing procedure). This time course by removes was given by Rapoport (1951), namely,

$$P(t+1) = \left[1 - \sum_{j=0}^{t} P(j)\right] [1 - e^{-aP(t)}], \tag{2}$$

where $P(t)$ is the fraction of *newly* contacted points. Then the total fraction of points contacted will be given by

$$x(t) = \sum_{j=0}^{t} P(j) \tag{3}$$

and the expected saturation fraction (ultimately contacted) by

$$x(\infty) = \sum_{j=0}^{\infty} P(j) = \gamma. \tag{4}$$

To test equation (2) in any field experiment, it is necessary actually to trace the rumor through the knowers at each remove. This was done in the C-ville experiment as described by Stuart C. Dodd (1952). In applying the data of the experiment to equation (2), two corrections had to be made. First, since in the tracing procedure only the actual *knowers* of the rumor were traced, the number of knowers had to be multiplied by the average fraction of knowers who became tellers. Second, the quantity a (the average number of hearers who became tellers) was not constant throughout the process but declined steadily at each remove.

With these corrections taken into account and with the actually observed (corrected) values of a substituted into each recursion indicated by equation (2), the comparison shown in Table I between predicted and observed numbers of tellers at each remove was obtained.

If, on the other hand, instead of taking the corrected values of a as

TABLE I

Remove	Tellers (Observed)	Tellers (Predicted)
0	42 (starters)	42
1	111	125
2	164	173
3	178	184
4	180	185
5	184	186

calculated from actual observations, one assumes a simple decreasing function of a to give the best fit for equation (2), namely,

$$a = \frac{13.5}{5+t}, \tag{5}$$

one obtains a better correspondence between observed and corrected numbers of tellers, as shown in Table II.

TABLE II

Remove	Tellers (Observed)	Tellers [By formulas (2) and (5)]
0	42	42.0
1	111	111.6
2	164	162.8
3	178	179.9
4	180	183.5
5	184	184.1

Without further experimentation, nothing can be said concerning either the significance of formula (5) or the excellent agreement between theory and experiment which it gives.

Our task in this paper is to derive a method for translating the time course by removes formula into an ordinary (continuous) time course formula. Obviously, the work in tracing a rumor through all the knowers, hearers, and tellers is an enormous one, and without it formula (2) is of no use in an experimental situation. Before we proceed to derive the transla-

tion of (2) into an ordinary clock time course equation, we shall give another expression somewhat more general than (2) and simpler. Starting with equation (11) of Solomonoff and Rapoport *loc. cit.*, we have

$$y(t+1)\left(1-\frac{1}{N}\right)^{ay(t)} = \text{constant} = K. \tag{6}$$

Here $y(t)$ is the number of non-knowers at the tth remove. We introduce a change of notation, in which y will now stand for the *fraction* of non-knowers, and K for the appropriately modified constant. This gives

$$y(t+1)\left(1-\frac{1}{N}\right)^{aNy(t)} = K. \tag{7}$$

For very large N, this can be written as

$$y(t+1)\ e^{-ay(t)} = K. \tag{8}$$

To evaluate K we note that if $x(t)$ is the fraction of knowers, so that $y(t) = 1 - x(t)$, we have

$$y(0) = 1 - x_0; \qquad y(1) = (1 - x_0)\ e^{-ax_0} \tag{9}$$

where x_0 is the initial fraction of knowers. Thus

$$K = (1 - x_0)\ e^{-a}. \tag{10}$$

Equation (7) then becomes, in terms of $x(t)$,

$$x(t+1) = 1 - (1 - x_0)\ e^{-ax(t)}, \tag{11}$$

which is simpler and more general than Rapoport's formula (2). It is an immediate consequence of (11) that γ must satisfy equation (1) if $x_0 = 0$.

Equation (11) holds only if a is independent of t. If a is a function of t, the more general formula (2) still holds.

We will now show that if the distribution of the time intervals between "hearings" and "tellings" is known, the clock time course of the rumor spread can be expressed in terms of the $x(j)$ and the parameters of the distribution.

Call the interval between each time an individual has heard the rumor for the first time and the time he has told it (not necessarily for the first time) a "telling interval." Suppose that we have a list of all the telling intervals in the process studied. Further, suppose that $g(\tau)$ is a function such that $g(\tau)d\tau$ represents the probability that a telling interval will have a length between τ and $\tau + d\tau$. Thus g(τ) is a probability density and the corresponding (accumulative) probability distribution

$$G(t) = \int_0^t g(\tau)\, d\tau \tag{12}$$

represents the probability that a telling has occurred by the time t following a hearing. If $r(1)$ is the fraction of the population who first learned of the rumor in the first remove, we see that $r(1)G(t)$ represents the fraction of that fraction completed by the time t. We now seek the probability distribution of the lengths of *chains* of telling intervals. If $G_n(t)$ is the probability distribution of the lengths of chains composed of n telling intervals, then we have, under certain assumptions to be stated below,

$$G_n(t) = G^* \ldots {}^*G(t), \tag{13}$$

where the operator on t is the n-fold convolution of G, defined by the iterative operation

$$G_n(t) = \int_0^t G_{n-1}(t-\tau)G'(\tau)\,d\tau. \tag{14}$$

Then, if $r(n)$ is the fraction of the population who become knowers on the nth remove, and $f(t)$ is the fraction who are knowers by the time t, we must have

$$f(t) = \sum_{n=0}^{\infty} r(n)G_n(t) = x_0 + \sum_{n=1}^{\infty} [x(n) - x(n-1)]G_n(t), \tag{15}$$

which is the ordinary time course formula desired.

The justification of formula (13) depends on the assumptions that the individuals act independently of each other and that the tellings of each individual are independent. Then the telling intervals will be formed independently and according to some distribution $G(t)$ which will remain constant for all removes. The distributions $G_n(t)$ are then the probability distributions of the sum of n independent random variables, each having the probability distribution $G(t)$.

Another way of looking at it is to consider the number of knowers N_n on the nth remove. Since chains of telling intervals are traced from each knower through the first individual who told this knower and so on back to the starters, we see that each knower has a *unique* chain of telling intervals connecting him to a starter. Thus N_n is also the number of such chains of n intervals. Hence $N_nG_n(t)$ is the expected number of such chains of length t or less. By the one to one relation between these chains and the knowers, $N_nG_n(t)$ is also the number of knowers on the nth remove at time t. If N is the total population, we have for the fraction of knowers at time t

$$\sum_{n=0}^{\infty} N_nG_n(t)\,N^{-1} = \sum_{n=0}^{\infty} r(n)G_n(t) \tag{16}$$

and the total fraction of knowers by the time t is thus given by (15).

We will now derive the time course equation for a special case,* namely, where

$$g(\tau) = k e^{-k\tau}. \tag{17}$$

Then

$$G(t) = G_1(t) = \int_0^t k e^{-k\tau} d\tau = 1 - e^{-kt}. \tag{18}$$

Similarly,

$$G_2(t) = \int_0^t G_1(t-\tau)\, dG_1(\tau) = G_1(t) - kt e^{-kt}, \tag{19}$$

$$G_3(t) = G_2(t) - \frac{k^2t^2}{2!} e^{-kt}. \tag{20}$$

An easy induction reveals that

$$G_{n+1}(t) = G_n(t) - \frac{k^n t^n}{n!} e^{-kt} = 1 - e^{-kt}E_n(kt), \tag{21}$$

where $E_n(kt)$ is the partial expansion of e^{kt} to the nth power inclusive. We further define $E_{-n}(kt) = 0$ for $n > 0$ and note that $E_0(kt) = 1$. Thus also $G_0(t) = 1$. Our equation (15) reduces for the special case of the decaying exponential frequency distribution of telling intervals to

$$f(t) = \sum_{n=0}^{\infty} r(n)\,[1 - e^{-kt}E_{n-1}(kt)]. \tag{22}$$

But

$$\sum_{n=0}^{\infty} r(n) = \gamma,$$

where γ is the saturation frequency as above. Thus we can write (22) as

$$f(t) = \gamma - e^{-kt} \sum_{n=0}^{\infty} r(n) E_{n-1}(kt). \tag{23}$$

We shall now investigate some of the properties of this function. We have

$$\begin{aligned} f'(t) &= k e^{-kt} \sum_{n=1}^{\infty} r_n [E_{n-1}(kt) - E_{n-2}(kt)] \\ &= k e^{-kt} \sum_{n=1}^{\infty} r_n \frac{(kt)^{n-1}}{(n-1)!}. \end{aligned} \tag{24}$$

* Recent data obtained at the Washington Public Opinion Laboratory (unpublished) indicate that actual distributions of telling intervals resemble the form we are considering.

Clearly $f'(t) \geqq 0$ for all $t \geqq 0$, as, of course, should be the case. Furthermore,

$$f''(t) = k^2 e^{-kt}\left[-r_1 + \sum_{n=1}^{\infty} r_{n+1} \frac{(kt)^{n-1}}{(n-1)!}\left(1 - \frac{kt}{n}\right)\right]. \tag{25}$$

Consider the last expression in the bracket. This is positive for $0 \leq t < 1/k$. On the other hand, for any n_0 there exists a t_0 sufficiently large such that

$$\left(1 - \frac{kt}{n}\right) \leq 0 \quad \text{for} \quad n \leq n_0 \quad \text{and} \quad t \geq t_0. \tag{26}$$

Since

$$\sum_{n=1}^{\infty} r_{n+1} \frac{(kt)^{n-1}}{(n-1)!}\left(1 - \frac{kt}{n}\right)$$

is a convergent series, there exists an n_1 such that

$$\left| \sum_{n=1}^{n_1} r_{n+1} \frac{(kt)^{n-1}}{(n-1)!}\left(1 - \frac{kt}{n}\right)\right| > \left| \sum_{n_1+1}^{\infty} r_{n+1} \frac{(kt)^{n-1}}{(n-1)!}\left(1 - \frac{kt}{n}\right)\right|. \tag{27}$$

If we choose n_0 so large that $n_0 > n_1$, then for the value of t_0 mentioned above and for all greater values of t, we shall have

$$\sum_{n=1}^{\infty} r_{n+1} \frac{(kt)^{n-1}}{(n-1)!}\left(1 - \frac{kt}{n}\right) < 0. \tag{28}$$

Thus this expression increases at first, reaches a maximum and decreases. Let it reach the maximum value M at t_1. Then if $M < r_1$, we see that $f''(t)$ is always negative. If, however, $M > r_1$, then there exist two points t' and t'' such that $t' \leq t_1 \leq t''$ and $f''(t) \leq 0$ for $t \leq t'$ and for $t \geq t''$, and $f''(t) \geq 0$ for $t' < t < t''$. The graph of such a function $f(t)$ is shown in Figure 1.

Note that if r_1 is sufficiently small, the initial period of negative second derivative is negligible and we have practically a sigmoid curve. On the other hand, if r_1 is sufficiently large, $f(t)$ loses its inflection points and becomes a "fall-away" curve. In fact, since the expression within the bracket in equation (25) can be written as

$$\sum_{j=2}^{\infty} \frac{(kt)^{j-2}}{2!}(r_j - r_{j-1}),$$

we see that we shall always have a "fall-away" time course curve under our present assumption on $g(\tau)$ if $r_1 \geq r_2 \geq r_3 \ldots$ etc., i.e., if the ordinal

time course curve traced through the data obtained by removes is also a "fall-away" curve.

If $g(\tau)$ is a normal frequency distribution, with mean m and standard deviation σ, i.e.,

$$g(\tau) = \frac{1}{\sigma\sqrt{2\pi}} e^{[-(\tau-m)^2/2\sigma^2]}, \tag{29}$$

the successive convolutions will be given by

$$\begin{aligned} G_1(t) &= \int_{-\infty}^{t} \frac{1}{\sigma\sqrt{2\pi}} e^{[-(\tau-m)^2/2\sigma^2]} d\tau \\ G_2(t) &= \int_{-\infty}^{t} \frac{1}{\sigma\sqrt{4\pi}} e^{[-(\tau-2m)/4\sigma^2]} d\tau \\ &\vdots \\ G_n(t) &= \int_{-\infty}^{t} \frac{1}{\sigma\sqrt{2n\pi}} e^{[-(\tau-nm)^2,2n\sigma^2]} d\tau . \end{aligned} \tag{30}$$

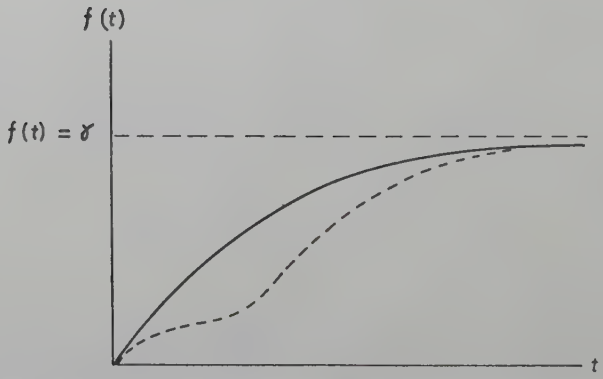

FIGURE 1. Solid line represents the time course of rumor spread for the case $r_1 > M_1$, where

$$M = \text{Max} \sum_{n=1}^{\infty} r_{n+1} \frac{(kt)^{n-1}}{(n-1)!}\left(1 - \frac{kt}{n}\right)$$

with respect to t. Dotted line represents the case $r_1 < M$.

The integrals (30), being generally available in tabulated form,* the values of $f(t)$ can easily be obtained in this case from equation (15), if the r_n's are known.

We note further that

$$f'(t) = \sum_{n=0}^{\infty} r_n G_n'(t) . \tag{31}$$

* The contributions to the integrals from negative values of t are meaningless but also negligible if the mean m is sufficiently large and σ not too large.

Again $f' \geq 0$ for all t, as should be the case. Also

$$f''(t) = \frac{1}{\sigma\sqrt{2\pi}} \sum_{n=1}^{\infty} \frac{r_n}{\sqrt{n}} e^{[-(t-nm)^2/2n\sigma^2]} \frac{(nm-t)}{2n\sigma^2}. \qquad (32)$$

Here, regardless of the values of r_n (provided they are convergent), $f''(t) \geq 0$ for t sufficiently small and $f''(t) < 0$ for t sufficiently large. The question of whether and how f'' changes sign in the intermediate region remains open.

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THE DONNAN EQUILIBRIUM

J. H. Bartlett and R. A. Kromhout
Department of Physics, University of Illinois
Urbana, Illinois

A complete solution has been obtained for the distribution of ions and for the electrostatic potential in a simple Donnan equilibrium, namely, where the membrane is permeable to two ions, but not to the third. Electrical neutrality is shown to be an extremely good approximation everywhere except close to the membrane.

If a system contains a membrane which is permeable to some ions but not to others, it will finally settle down into an equilibrium state where the relative concentrations of the ions on the two sides are markedly different

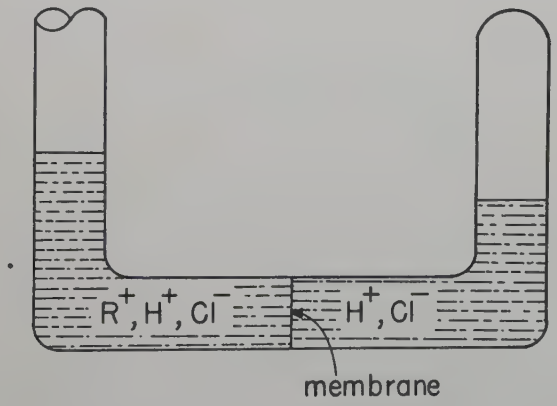

Figure 1. System with semi-permeable membrane

from what they would be if no membrane were present. The ions which cannot go through the membrane exert electrical forces on those which can, and it is this that causes the difference.

In order that equilibrium be achieved, let us suppose that the membrane (which is imagined to be a geometrical plane, i.e., of zero thickness) spans the cross-section of a vessel as shown in Figure 1. This vessel is closed on one side, and open to the atmosphere on the other. Since, at equilibrium, the concentrations are different, the level of the solution will not be the same on one side as on the other.

For simplicity, suppose that there are just three types of ion present, namely, R^+, H^+, and Cl^-, and that the membrane is permeable to H^+ and Cl^- but not to R^+. (One could take into account the difference of osmotic pressure on the two sides of the membrane [Guggenheim, 1949], but the solution will be regarded as so dilute that this effect is negligible, and also so dilute that activity can be replaced by concentration.) Initially, a known amount of RCl is put in solution on one side of the membrane, and a known amount of HCl is put in anywhere. Our problem is then to find the equilibrium concentrations of the ions as a function of the distance.

In this paper we shall show that this problem has a solution which satisfies the following conditions: (a) the electrostatic potential V and its first derivative are continuous everywhere; (b) the electric intensity $-(dV/dx)$ is zero at the walls $x = -L, +L$; (c) the electrochemical potential energy, per mole, of each ion is a constant; and (d) Poisson's equation is obeyed.

The mathematical expression of condition (c) for the ith ion type is

$$RT \ln c_i + z_i F V = \text{Const.}, \tag{1}$$

where

R = gas constant per mole .

T = absolute temperature ,

c_i = concentration of ith ion , $i = 1$ refers to H^+
$i = 2$ to Cl^- , $i = 3$ to R^+

z_i = valence of ith ion ,

F = Faraday .

Equation (1) may also be written as

$$c_i = c_{ia} e^{(-z_i F V/RT)}, \tag{2}$$

where c_{ia} is the concentration when $V = 0$. Let the position of the membrane be $x = 0$, and let $V = 0$ at $x = -L$.

Poisson's equation is, if D = dielectric constant,

$$\frac{d^2 V}{(dx^2)} = -\frac{4\pi F}{(D)} \sum_{i=1}^{3} z_i c_i . \tag{3}$$

Substitution of (2) into (3) yields

$$\frac{d^2 V}{dx^2} = \kappa (e^{aV} - l e^{-aV}),$$

where

$$\kappa = \frac{4\pi F}{D} c_{2a}, \qquad \kappa l = \frac{4\pi F}{D} (c_{1a} + c_{2a}), \qquad a = \frac{F}{RT}. \tag{4}$$

On integration, we have

$$\left(\frac{dV}{dx}\right)^2 = \frac{2\kappa}{a}\left(e^{aV} + l e^{-aV} + A\right). \tag{5}$$

If we require condition (b) that $(dV/dx) = 0$ at $x = -L$, then, from (5), $A = -l - 1$. The quantity $l - 1$ may be positive or negative; let us study the case $l > 1$. Then, from (4), at $x = -L$, $(d^2V/dx^2) < 0$. This means that $V < 0$ near $x = -L$. From (4), we see that $(d^2V/dx^2) < 0$ as long as $V < 0$ and $l > 1$. Hence V is always negative and bending away from the x-axis, at least up to the membrane. After the membrane is crossed, there is no longer any R^+ ion, which means that l must be replaced by a different constant l_0. Then, as we shall show, V can bend back toward the x-axis, to become asymptotic to a negative value V_0 at $x = +L$. The charge density $\rho = -(D/4\pi)\,(d^2V/dx^2)$ will then be positive for $x < 0$ and negative for $x > 0$. The total charge is $\int \rho\, dx = -(D/4\pi)\Delta(dV/dx)$. This will be zero if dV/dx equals zero at $x = -L$ and $x = +L$, and the solution will be electrically neutral on the whole.

Let us now integrate (5) for the general case where $(dV/dx) = 0$ when $V = V_0$. We set $\tau^2 = e^{aV}$, and $\tau_0^2 = e^{aV_0}$. Then we find:

$$-A_0 = \tau_0^2 + \left(\frac{l_0}{\tau_0^2}\right). \tag{6}$$

Equation (5), on rearrangement, becomes

$$\begin{aligned} dx &= \pm\sqrt{\frac{2}{\kappa a}}\,\frac{d\tau}{\sqrt{\tau^4 + a_0\tau^2 + l_0}} \\ &= \pm\sqrt{\frac{2}{\kappa a}}\,\frac{d\tau}{\sqrt{(\tau^2 - \tau_0^2)\left[\tau^2 - \dfrac{l_0}{\tau_0^2}\right]}}. \end{aligned} \tag{7}$$

Now the elliptic integral of the first kind is (Jahnke-Emde, 1938)

$$u = F(\varphi, k) = \int_0^{\varphi} \frac{d\psi}{\sqrt{1 - k^2\sin^2\psi}} = \int_0^{\sin\varphi} \frac{d\tau}{\sqrt{(1-\tau^2)(1-k^2\tau^2)}}.$$

Integration of (7) gives us

$$x - x_0 = \pm\sqrt{\frac{2}{\kappa a l_0}}\,\tau_0 u\left(\sin^{-1}\frac{\tau}{\tau_0},\ \frac{\tau_0^2}{\sqrt{l_0}}\right)$$

and, therefore,

$$V - V_0 = \pm\frac{2}{a}\ln\,\mathrm{sn}\left[\pm\sqrt{\frac{\kappa a l_0}{2}}\,\frac{x - x_0}{\tau_0},\ \frac{\tau_0^2}{\sqrt{l_0}}\right]. \tag{8}$$

The sn function is 0 at $x = x_0$ and again at

$$\sqrt{\frac{\kappa a l_0}{2}}\,\frac{x - x_0}{\tau_0} = 2K \equiv 2F\left(\frac{\pi}{2},\ k\right).$$

In order to keep V finite, we must have

$$\sqrt{\frac{\kappa a l_0}{2}}\,\frac{x - x_0}{\tau_0} < 2K = 2\int_0^{\pi/2} \frac{d\varphi}{\sqrt{1 - k^2 \sin^2 \varphi}}. \tag{9}$$

Let $k' = \sqrt{1 - k^2}$.

From (9), if L = length of the region,

$$2K\tau_0 > L\left[\frac{F}{2RT}\,\frac{4\pi F}{D}\,(c_{1a} + c_{3a})\right]^{1/2}. \tag{10}$$

As an extreme case, assume $L = 10^{-4}$ cm, and $c_{1a} + c_{3a} = 10^{-4}$ mol/liter $= 10^{-7}$ mol/cc. The constants are taken to be

$D = 80$, $\quad F = 2.895 \times 10^{14}$ e.s.u.,

$$R = 8.315 \times 10^7 \text{ erg} \mid \text{deg} \mid \text{mol}, \qquad T = 300^0.$$

Substituting in (10), we find

$$K\tau_0 > 8.12. \tag{11}$$

First, consider the region to the left of the membrane, and use equation (8), with

$$\tau_0 = 1 \text{ and } k = \frac{1}{\sqrt{l_0}}.$$

For a value of K as great as 8 [inequality (11)], it is seen from tables that k is nearly unity (Jahnke-Emde, *loc. cit.*, p. 85). In the region (Jahnke-Emde, p. 73),

$$K \cong \ln\frac{4}{\sqrt{1 - k^2}}; \qquad l_0 - 1 \cong \frac{1}{16}\, e^{-16.2}.$$

Thus, the value of l_0 is very close to unity, which means that the solution is practically electrically neutral at $V = 0$. The same argument applied to equation (8) for $\tau_0 = 1$ demands that $\tau_0^2\sqrt{l_0 = 1}$. The concentration of positive ions at V_0 is measured by l_0/τ_0^2 and the concentration of negative ions by τ_0^2, so that these two concentrations are again very nearly equal at $V = V_0$. If we put $l_0 = 1$ in (8), then, if $\tau_0 = 1$,

$$\begin{aligned} V &= \pm\frac{2}{a} \ln \tanh\left[\pm\sqrt{\frac{\kappa a}{2}}\,(x - x_0)\right] \\ &= \pm\frac{2}{a} \ln \tanh u = \frac{2}{a} \ln y, \end{aligned} \tag{12}$$

if $u = \pm\sqrt{\kappa a/2}\,(x - x_0)$ and $y = \tanh u$.

The region within which the potential varies turns out (see below) to be of the order of 300 A.U. in length. Since L is assumed greater than 10^{-4} cm, it may in this approximation be regarded as infinite.

Designate the regions to the right and left of the membrane with the subscripts r and l, respectively. Let us try to fit smoothly two solutions of type (12), namely,

$$V = \frac{2}{a} \ln \tanh \left[-\sqrt{\frac{\kappa_l a}{2}} (x - x_1) \right], \qquad x < 0, \tag{13}$$

$$V - V_0 = -\frac{2}{a} \ln \tanh \left[+\sqrt{\frac{\kappa_r a}{2}} (x - x_2) \right], \qquad x > 0. \tag{14}$$

The first solution vanishes at $x = -\infty$, and the second solution vanishes at $x = +\infty$. Set

$$u_l = \sqrt{\frac{\kappa_l a}{2}} (x_1 - x)$$

and

$$u_r = \sqrt{\frac{\kappa_r a}{2}} (x - x_2).$$

Then

$$\begin{aligned} \left.\frac{dV}{dx}\right|_l &= \frac{2}{a} \coth u_l \operatorname{sech}^2 u_l \frac{du_l}{dx} \\ &= -\sqrt{\frac{2\kappa_l}{a}} \frac{1 - y_l^2}{y_l}, \qquad x < 0, \\ \left.\frac{dV}{dx}\right|_r &= -\frac{2}{a} \coth u_r \operatorname{sech}^2 u_r \frac{du_r}{dx} \\ &= -\sqrt{\frac{2\kappa_r}{a}} \frac{1 - y_r^2}{y_r}, \qquad x > 0. \end{aligned} \tag{15}$$

From (13), $V_l = (2/a) \ln y_l$ and $V_r - V_0 = -(2/a) \ln y_r$.

Equating V_l and V_r at $x = 0$,

$$V_0 = \frac{2}{a} \ln y_l y_r \qquad \text{or} \qquad v_l y_r = \tau_0. \tag{16}$$

(Note: $1/a = RT/F = .862 \times 10^{-4}$ e.s.u. $\cong 26$ m.v.)

Also equating $dV/dx|_l$ and $dV/dx|_r$ at $x = 0$ and using (14) and (16),

$$1 - v_l^2 = y_l^2 - \tau_0^2,$$

$$v_l^2 = \frac{1 + \tau_0^2}{2} = \frac{1.02136}{2}, \qquad v_l = .71466,$$

if V_0 be taken as -100 m.v. for definiteness.

We now find:

$$\gamma_r = \frac{\tau_0}{\nu_l} = \frac{.14615}{.71466} = .2045; \quad u_l = .897,$$

$$u_r = .2075,$$

$$V(x=0) = 52 \ln .7146.$$

Thus, the value of V at $x = 0$ is -17.47 m.v. if $V_0 = -100$ m.v.

Concentrations. Suppose that at $V = 0$, $[Cl^-]_{-\infty} = 0.1$ mols/liter. Then at $V = -100$ m.v., $[Cl^-]_{\infty} = 0.1\ e^{-100/26} = 2.136 \times 10^{-3}$. Because of electrical neutrality, $[H^+]_{+\infty} = 2.136 \times 10^{-3}$.

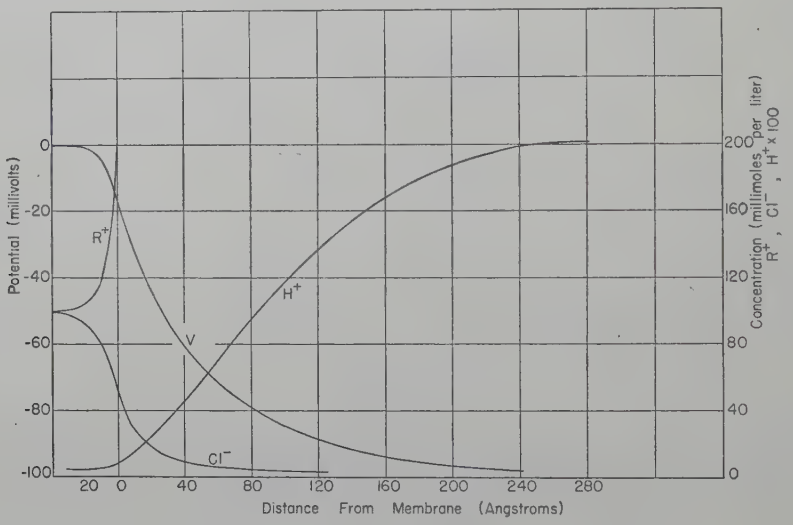

FIGURE 2. Potential and concentrations vs. distance

At $V = 0$, $[H^+]_{-\infty} = 2.136 \times 10^{-3} \times e^{-100/26} = 4.56 \times 10^{-5}$. Again due to electrical neutrality, $[R^+]_{-\infty} = 0.1 - (4.56 \times 10^{-5})$.

For

$$x < 0,\ x = 19.5\,(.897 - u)\ \text{Å},$$

$$x > 0,\ x = 133.2\,(u - .2045)\ \text{Å}.$$

Let δ_r be that value of u such that:

$$-100 - V(\delta_r) = \frac{1}{e}[-100 - V(u_r)]. \tag{17}$$

Similarly for δ_l:

$$0 - V(\delta_l) = \frac{1}{e}[0 - V(u_l)], \tag{18}$$

or

$$V(\delta_l) = \frac{1}{e}(-17.17) = -6.31 \text{ m.v.},$$

$$V(\delta_r) = -100 + 30.45 = -69.55 \text{ m.v.}$$

From (17) and (18), the potential thus decreases to 1/e of its value in 59.4 Å if $x > 0$ and in 9.6 Å if $x < 0$.

We may then define the "double-layer" thickness δ at the membrane:

$$\delta = \delta_l + \delta_r = 69 \text{Å} .$$

Thus the "double-layer" contains $28.26 \times 6.023 \times 10^{23} \times 1.7 \times 10^{13}$ ions/cm^2, or a cell of volume δ^3 in this "double-layer" contains about 10 ions on the average. This means that any use of a macroscopic theory for nonequilibrium calculations—where long time averages of C, V, and their derivatives cannot be assumed—would be of doubtful validity.

Figure 2 shows how the concentrations of the various ions, and the potential V, vary as a function of distance. This presents then the solution of the Donnan equilibrium problem.

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AWARDS FOR POST-DOCTORAL STUDY IN STATISTICS AT THE UNIVERSITY OF CHICAGO

Three $4000 post-doctoral fellowships in Statistics are offered for 1953–54 by the University of Chicago. The purpose of these fellowships, which are open to holders of the doctor's degree or its equivalent in research accomplishment, is to acquaint established research workers in the biological, physical, and social sciences with the crucial role of modern statistical analysis in the planning of experiments and other investigative programs, and in the analysis of empirical data. The development of the field of Statistics has been so rapid that most current research falls far short of attainable standards, and these fellowships (which represent the third year of a five-year program supported by The Rockefeller Foundation) are intended to help reduce the lag by giving statistical training to scientists whose primary interests are in substantive fields rather than in Statistics itself. The closing date for applications is February 1, 1953; instructions for applying may be obtained from the Committee on Statistics, University of Chicago, Chicago 37.

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